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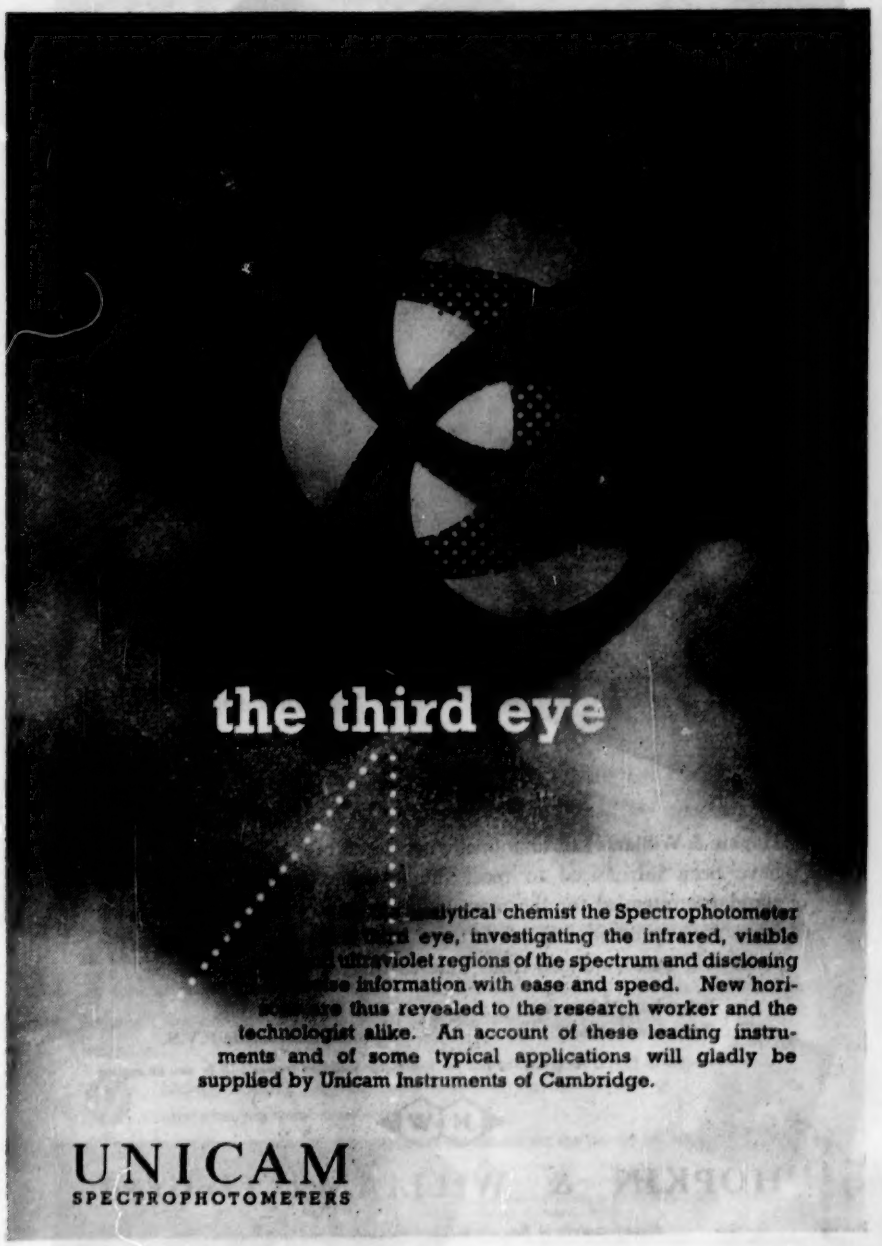
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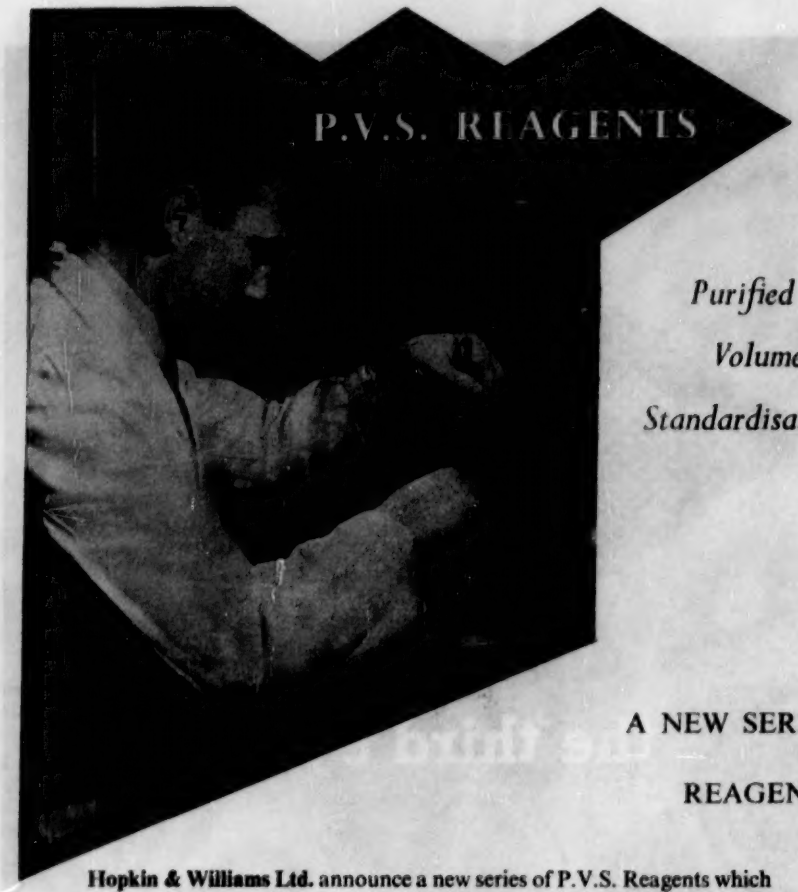

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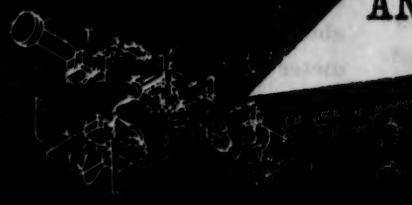

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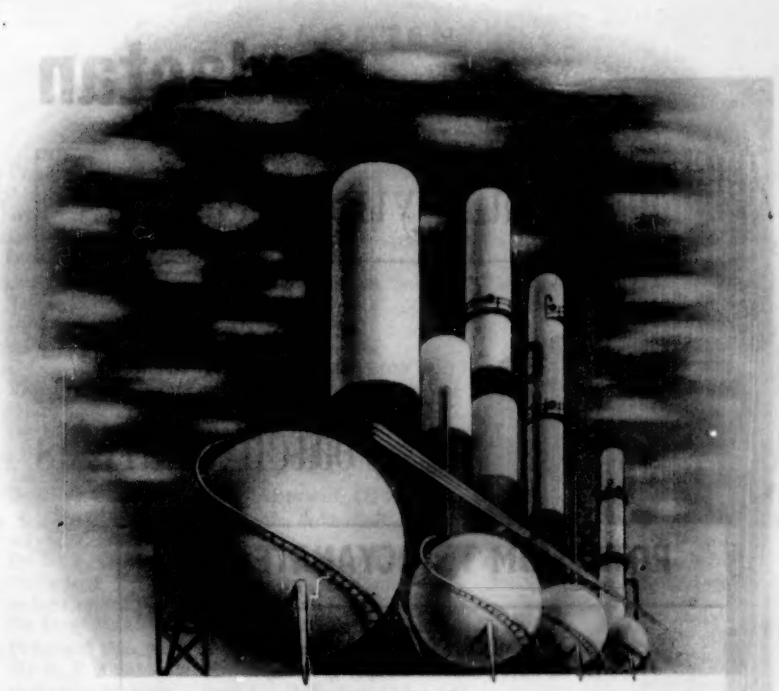

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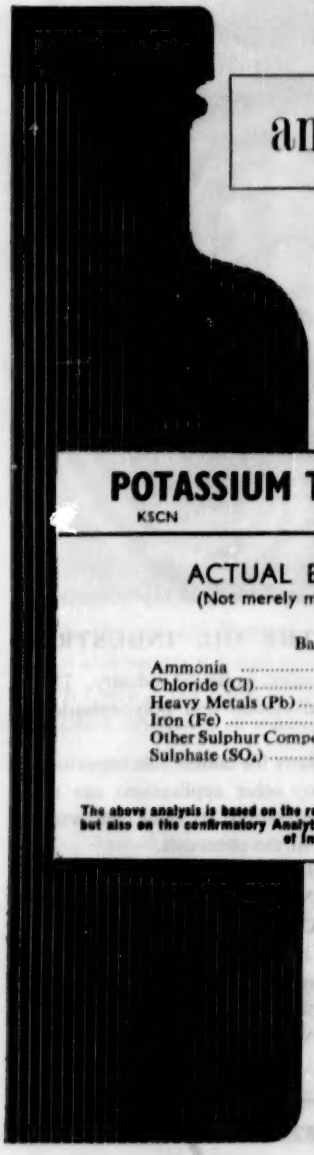

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Ammonia	no reaction
Chloride (Cl)	0·003%
Heavy Metals (Pb)	0·00025%
Iron (Fe)	0·0001%
Other Sulphur Compounds	0·0002%
Sulphate (SO_4)	0·0006%

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Electronic Spectra, Hyperconjugation, and the Baker–Nathan Effect.

By A. Burawoy and E. Spinner.

[Reprint Order No. 6064.]

The spectra of diphenyl, acetophenone and its oxonium salt formed in concentrated sulphuric acid, aniline, the phenoxide ion and some of their 4-alkyl derivatives are determined. The varying effect of the alkyl groups on the *K*-bands shows that their electron-donating character increases in the normal inductive order Me < Et < Pr^{i} < Bu^{t} and that the differences between the alkyl groups are enhanced with the increase of electron demand. The absence in electronic spectra of a hyperconjugative electron-release increasing in the order Bu^{t} ⟶ Me is discussed.

It has been pointed out recently that the Baker–Nathan effect is encountered only in chemical equilibria and other changes in which bond contractions and bond stabilizations within one of the two entities involved play an important part, that in contrast it is not observed in physical properties such as dipole moments, ionization potentials and, anticipating the present investigation, electronic spectra which do not involve bond contractions, and that, in our view, it cannot be accounted for by the conception of hyperconjugation which moreover is not required for its interpretation (Burawoy and Spinner, *J.*, 1954, 3752).

The influence of substituents on light absorption is of considerable complexity, being dependent on both their position and the type of the electronic transition involved, *i.e.*, the type of absorption band under consideration [for their classification as *R*-, *K*-, and *B*(benzenoid)-bands, see Burawoy, *Ber.*, 1930, **63**, 3155; 1931, **64**, 464, 1635; 1932, **65**, 941; *J.*, 1939, 1177; *Discuss. Faraday Soc.*, 1950, **9**, 70]. Qualitatively, the *K*-bands of high intensity are best understood. They are due to transitions involving electron migrations (perturbations) along the (axis of) conjugated systems (I) (cf., *e.g.*, McMurry and Mulliken, *Proc. Nat. Acad. Sci.*, 1940, **26**, 312, and earlier papers; Calvin and Lewis, *Chem. Rev.*, 1939, **25**, 303). One important factor determining the position of a *K*-band is the polarity of such systems, *i.e.*, influences increasing their polarity (in the ground state) facilitate the electron migration and displace the *K*-band to longer wavelengths. It could be, therefore, expected that an investigation of the effect of terminal alkyl groups (I; A or B) of certain conjugated systems on the position of the corresponding *K*-bands would give information about the order of electron release by alkyl groups in the ground state (as well as in the excited state).

(I) A·[CH:CH]$_n$·B ⟶ (II) *p*-R·C$_6$H$_4$·COMe ⟶ *p*-R·C$_6$H$_4$·CMe:$\overset{+}{\text{O}}$H (III)

The *K*-bands of the alkylbenzenes (at approximately 2000 Å) in heptane solution have been measured by Platt and Klevens (*Chem. Rev.*, 1947, **41**, 301; *J. Chem. Phys.*, 1948, **16**, 832). They appear, unfortunately, only as shoulders superposed on the slope of the bands of higher intensity (maxima near 1850 Å) probably due to Rydberg transitions (for interpretations of this band system and relevant literature, see Hammond, Price, Teegan, and Walsh, *Discuss. Faraday Soc.*, 1950, **9**, 53; Burawoy, *ibid.*, p. 78), and the positions of the true maxima are uncertain. We have, therefore, determined the spectra of diphenyl and 4-methyl- and 4-*tert.*-butyl-diphenyl in hexane and alcohol. The *K*-bands show a slight, but definite red-shift from the methyl to the *tert.*-butyl homologue.

Brown and Reagan (*J. Amer. Chem. Soc.*, 1947, **69**, 1033) have already observed that (in *iso*octane) the *K*-band of *p-tert.*-butylnitrobenzene lies at slightly longer wavelengths than that of its methyl homologue. We have now found that the *K*-bands of the four 4-alkylacetophenones (II) in hexane and those of their oxonium salts (III) in concentrated sulphuric acid behave similarly and, in particular, that the red-shifts increasing in the order Me < Et < Pr^{i} < Bu^{t} are appreciably greater for the oxonium ions than for the ketones.

After completion of this investigation, Sweeney and Schubert (*ibid.*, 1954, **76**, 4625)

reported a similar investigation of the *p*-alkylbenzoic acids, 4-alkylacetophenones, and *p*-alkylnitrobenzenes in alcohol and the oxonium salts of the ketones and nitro-compounds in sulphuric acid. Their data for the ketone oxonium ions are in very good agreement with ours; their values for the ketones and nitro-compounds, on the other hand, indicate no shift from the methyl to the *tert.*-butyl derivative, contrary to Brown and Reagan's and our observations, but those for the benzoic acids show again the normal red-shift in the order Me ⟶ Bu^t. Our original determinations were carried out with a Hilger E3 quartz spectograph fitted with a Spekker photometer. The plates were carefully analysed and, although the absolute differences may be subject to some experimental error, the direction and order of the displacements in each series is certain. After appearance of Sweeney and Schubert's note, we also examined the spectra of 4-methyl- and -*tert.*-butyl-acetophenone in hexane and alcohol and those of the diphenyls in alcohol with a Hilger Uvispek Photoelectric Spectrophotometer, originally not available, and confirmed the general trend. Our results are reproduced in Table 1 together with Brown and Reagan's data for the nitro-compounds.

The position of the *K*-bands of all substances discussed so far is determined by the facility of the electron migrations along the axis of the absorbing conjugated system, proceeding from the alkyl group into the benzene ring as indicated in (II) and (III). The results discussed clearly indicate that the polarity of the absorbing system (in the ground state) increases in the inductive order Me < Et < Pr^i < Bu^t and, what is most important, that the differences are greatest in the ions, in which the electron demand on the alkyl groups is greatest. Moreover, the results show that, in spite of the greater electron demand in the excited state as compared with the ground state, the relative stability of the excited states also increases in the order Me ⟶ Bu^t, and more so in the oxonium ions than in the ketones.

TABLE 1. *Maxima of K-bands of compounds p-*R·C$_6$H$_4$·X.

	R:	H		Me		Et		Pr^i		Bu	
X	Solvent	λ	$10^{-3}\varepsilon$	λ	$10^{-3}\varepsilon$	λ	$10^{-3}\varepsilon$	λ	$10^{-3}\varepsilon$	λ	$10^{-3}\varepsilon$
NO_2	*iso*Octane *	2520	8·6	2640	10·3	—	—	2650	10·4	2650	10·7
COMe	C_6H_{14}	2387	12·5	2466	17·5	2470	17·0	2478	17·0	2478	20·0
"	" †	—	—	2472	16·2	—	—	—	—	2480	19·5
"	EtOH †	—	—	2516	14·5	—	—	—	—	2524	16·0
CMe:$\overset{+}{O}$H	H_2SO_4	2950	28·0	3113	30·0	3128	30·0	3150	32·0	3155	28·0
Ph	C_6H_{14}	2467	19·0	2513	19·1	—	—	—	—	2524	22·0
	EtOH †	—	—	2523	21·0	—	—	—	—	2534	21·0
NH_2	EtOH	2344	8·0	2355	10·0	—	—	—	—	2354	12·0
	" †	—	—	2362	10·0	—	—	—	—	2361	10·0
O^-	0·1N-NaOH	2345	11·0	2359	9·5	—	—	—	—	2357	13·0
	" †	—	—	2366	8·8	—	—	—	—	2364	11·5

* Brown and Reagan, *loc. cit.* † Determinations with Uvispek Photoelectric Spectrometer.

It should be noted, however, that the *K*-bands of the parent compounds are displaced appreciably to longer wavelengths by the introduction of a methyl group into the 4-position. This red-shift is only partly due to the increased polarity of the system (in the ground state). As will be fully discussed in a forthcoming publication, the greater polarizability of the Me–C electrons as compared with the H–C electrons, *i.e.*, the "extension" of the absorbing conjugated system, is another important factor facilitating the electron migration which is less important for substituents in the methyl group. In order to ensure that the electron-donating power of the alkyl groups (in the ground state) is the decisive factor for the absorption changes observed for the alkyl homologues, the *K*-bands of *p*-methylaniline and the *p*-methylphenoxide ion were compared with those of their *tert.*-butyl homologues (cf. Table 1). In these substances the alkyl groups are at the negative end of the absorbing conjugated system, and the electon displacement determining the position of the *K*-bands proceeds now into the alkyl group as indicated in (IV) and (V).

(IV) *p*-R·C$_6$H$_4$·NH$_2$ ⟵ *p*-R·C$_6$H$_4$·O$^-$ (V)

This is supported by the observation that the introduction of a methyl group in the *p*-position is responsible for much smaller red-shifts of the *K*-bands than in the substances discussed above. The polarity of the absorbing system in the direction of the electron migration determining the position of the *K*-band will now be reduced. This would result in a hypsochromic shift which, however, is masked by a slightly greater red-shift due to the increased polarizability of the Me–C electrons.

No significant difference in the position of the *K*-bands of the methyl and butyl homologues is observed, but the latter, certainly, do not absorb at longer wavelengths. It appears that the expected small hypsochromic displacement due to the change of polarity is partly or completely compensated by a red-shift due to the greater polarizability of the electron system of the Bu^t–C group.

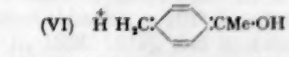
Matsen, Robertson, and Chuoke (*Chem. Rev.*, 1947, **41**, 273) have shown that the *B*-band systems of the alkylbenzene vapours are displaced to shorter wavelengths in the order Me ⟶ Bu^t and suggested that this was the spectroscopic analogue of the Baker–Nathan effect. Unfortunately, the effect of substituents on *B*-bands is complex and not well understood, but it may suffice to show that their positions in the spectra of monosubstituted benzenes cannot be taken as an indication of the polar effect of the substituents. This is illustrated in Table 2 by the maxima of the *B*-bands of the monohalogenobenzenes, phenol, and thiophenol which are compared with the corresponding *K*-bands. In contrast to the latter, the *B*-bands at least of iodobenzene and thiophenol are "anomalous." It appears that some unknown effect, which increases with the size of the substituent and may be of a steric nature but makes itself felt only in the electronic transition responsible for *B*-bands, causes displacements to shorter wavelengths. This matter requires further elucidation (cf. also Hammond, Price, Teegan, and Walsh, *loc. cit.*; Bowden, Braude, and Jones, *J.*, 1946, 948).

TABLE 2. *Maxima* (Å) *of B- and K-bands of compounds* $C_6H_5{\cdot}X$ *in alcohol.*

X	H *	F †	Cl †	Br †	I †	OH	SH
B-Band	2550	2540	2570	2610	2560	2730	2680
K-Band	2036	2040	2100	2100	2260	2105 *	2375

* Determinations in water by Doub and Vandenbelt, *J. Amer. Chem. Soc.*, 1947, **69**, 2714.
† Bowden and Braude, *J.*, 1952, 1068.

Discussion.—The hypothesis of an electromeric electron release by alkyl groups or of hyperconjugation was originally introduced to account for the Baker–Nathan effect (Baker and Nathan, *J.*, 1935, **519**, 1940) and later applied to the interpretation of the shortening and strengthening of the C_{Me}–C bonds in substances such as propyne and of the effect of alkyl groups in electronic spectra (Pauling, Springall, and Palmer, *J. Amer. Chem. Soc.*, 1939, **61**, 927; Mulliken, *J. Chem. Phys.*, 1939, **7**, 339; Mulliken, Rieke, and Brown, *J. Amer. Chem. Soc.*, 1941, **63**, 41; cf. also Price, *Chem. Rev.*, 1947, **41**, 257; Walsh, *Ann. Rep.*, 1947, **44**, 32; for further references, see Baker, "Hyperconjugation," Oxford, 1952; Coulson, "Valence," Oxford, 1952). An extension of the conception of non-localized bonds, it postulates an electron release in the order Bu^t ⟶ Me which should be greatest when the electron demand on the alkyl group is strongest. It should be equally observed in chemical and spectroscopic changes. For instance, the hyperconjugated structure (VI) should contribute more strongly to the true structure of the oxonium ion of 4-methylacetophenone than the structure (VII) to that of the ketone itself, and the contribution of (VI) and (VII) should be still greater in the excited states of both.

(VI)  (VII)

The results of the present and Sweeney and Schubert's spectroscopic investigation exclude the presence of a hyperconjugative electron release of alkyl groups in the order Bu^t ⟶ Me in both the ground and the excited states of the examined substances. This lends additional experimental support to the conclusion that the valency conception of

hyperconjugation does not account for the Baker–Nathan effect and the physical properties referred to above and, thus, its assumption is not required (Burawoy and Spinner, *loc. cit.*).

Shorter and Hinshelwood (*J.*, 1949, 4142), having found an indication of the Baker–Nathan effect in the rates of hydrolysis of the halides R·CMe_2Cl, have, in this instance, suggested that a steric inhibition of solvation due to the increasing congestion round the charged carbon atom in the carbonium ions formed might make some contribution to this effect. Sweeney and Schubert (*loc. cit.*), in order to account for the striking contrast between the effect of alkyl groups in chemical and spectroscopic changes, suggested that this factor is of general importance for the Baker–Nathan effect. However, it is difficult to see how inhibition of solvation could make any important contribution to the Baker–Nathan effect observed, *e.g.*, in the ionization of 4-alkylbenzyl bromides or 3-alkyl-1 : 1-dimethylprop-2-ynyl chlorides, in which systems the alkyl groups are appreciably removed from the centre of the developing charge. Moreover, the Baker–Nathan effect is also observed in the dissociation constants of the *p*-alkylbenzoic acids (Baker, Dippy, and Page, *J.*, 1937, 1774), although steric inhibition of solvation (of the anion) would only reinforce the effect due to the normal inductive order of the alkyl group.

We have ascribed the Baker–Nathan effect to a steric resistance to bond contraction and stabilization, *e.g.*, of the bond R–C, as enforced by an increased positive charge at C in one of the two entities partaking in a chemical change, contraction and stabilization being reduced with the increasing size of the alkyl group (for details, see Burawoy and Spinner, *loc. cit.*; Burawoy, "Contribution a l'Étude de la Structure Moléculaire," Desoer, Liège, 1947—48, p. 73).

This interpretation, in contrast to that based on hyperconjugation, involves only inductive electron displacements and does not require that the decreasing stabilization of the linkage R–C in the order Me–C ⟶ Bu^t–C is accompanied by a corresponding inversion of the order of the electron-donating powers of the alkyl groups or even of a reduction of their differences. In absence of any steric inhibition of bond contraction, an electron demand at the atom C would be responsible for an electron displacement increasing in the order Me–C ⟶ Bu^t–C, *i.e.*, the order of increasing polarizability of the systems. Our observations indicate that only the magnitude of these increases can be reduced by the steric inhibition of bond contraction.

In the past, interpretations of chemical and physical changes have been generally attempted in terms of polar effects and have proved, on the whole, to be successful in qualitative comparative discussions. However, equivalent changes of polarity of different linkages X–C involving different groups or atoms X (and possessing different bond energies) cannot be expected to be responsible for equal bond-energy changes, and it cannot be surprising that in isolated cases such as the Baker–Nathan effect (and possibly the similar behaviour of the halogen atoms in chemical changes, Burawoy, *op. cit.*, 1947—48) this relationship breaks down even qualitatively.

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The Red Colour given by Coal-tar Phenols and Aqueous Alkalis. Isolation of a Quinone derived from a Tetrahydroxytetramethyldiphenyl.

By Wilson Baker and D. Miles.

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The phenolic constituents of coal tar, particularly from low-temperature carbonisation processes, give red solutions in aqueous alkalis owing to simultaneous aerial oxidation of *C*-alkylated catechols and resorcinols. A study has been made of the red colouring matter derived from 3 : 5-dimethylcatechol and 2 : 4-dimethylresorcinol. Oxidative coupling of these phenols is limited by nuclear substitution, and gives in almost quantitative yield the crystalline monosodium salt of a quinone derived from 2 : 4 : 3′ : 4′-tetrahydroxy-3 : 5 : 2′ : 6′-tetramethyldiphenyl (III). The structure of (III) was established by Ullmann condensation of 4-iodo-3 : 5-dimethylveratrole and 2 : 4-dimethoxy-3 : 5-dimethyliodobenzene to 2 : 4 : 3′ : 4′-tetramethoxy-3 : 5 : 2′ : 6′-tetramethyldiphenyl (IX), subsequent demethylation and oxidation giving a quinone identical with that previously obtained.

The dihydroxyquinone derived from (III) might possess any of three different structures, and it is shown to be a tautomeric substance capable of reacting in the *o*-benzoquinonoid form (XII) and one or both of the diphenoquinone forms (X) and (XI). The effects of steric factors on the central carbon–carbon bond in these quinones are discussed.

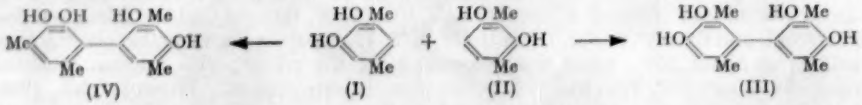
It has long been known that coal tars, particularly those prepared by the low-temperature carbonisation of coal, impart red-brown or red colours to aqueous solutions of alkalis. These red colours have been recognised as arising from aerial oxidation of phenolic material, and have proved an embarrassment in the manufacture of colourless and non-staining disinfectants and sheep dips, and even in the disposal of waste water from low-temperature plants. Gluud (*Ges. Abhandl. Kenntnis Kohle*, 1918, **3**, 66) thought that the colour was due to catechol, and Currey (*J. Soc. Chem. Ind.*, 1923, **42**, 379T) separated a phenolic fraction, distilling at about 250°, which was responsible for the colour; this fraction consisted principally of catechol, but other polyhydric phenols were present. Edwards (*ibid.*, 1924, **43**, 145T) suggested that an oxidation-condensation reaction of a phenol occurred, with production of a derivative of rosolic acid or of coumaranone. The oxidative nature of the process was clearly demonstrated by MacLeod, Chapman, and Wilson (*ibid.*, 1926, **45**, 401T), who concluded that the coloured compound resulted from "a benzenoid–quinonoid transformation with subsequent oxidation to a deeper coloured compound."

Burke and Caplan (*Ind. Eng. Chem.*, 1927, **19**, 34) showed that catechol itself was not responsible for the production of the red colour, but found that the active substance or substances could be separated from the phenolic fraction of low-temperature coal tar by extraction into aqueous borax (with which catechols form strongly acidic complexes), and regeneration therefrom and final distillation. They thus obtained a colourless oil of constant refractive index, b. p. 256°, which did not crystallise even at −20°; analyses and molecular weight agreed with a molecular formula $C_8H_{10}O_2$. It was concluded that this material was a homogeneous dimethylcatechol; the fluorescein test which it gave was thought to be due, not to a resorcinol, but to the dimethylcatechol itself. Burke and Caplan further concluded that as the compound was not the known solid 3 : 5- or 4 : 5-dimethylcatechol, it must be either 3 : 4- or 3 : 6-dimethylcatechol. The inadequacy of this suggestion became apparent when these two dimethylcathechols were synthesised. 3 : 6-Dimethylcatechol has m. p. 101° (Loudon and Scott, *J.*, 1953, 268; Baker, Bondy, Gumb, and Miles, *J.*, 1953, 1615), and 3 : 4-dimethylcatechol has m. p. 84—85° (Baker *et al.*, *loc. cit.*); both crystallise extremely easily and a 1 : 1 mixture of the two has m. p. about 65°. Moreover, 3 : 6-dimethylcatechol gives a purple colour when oxidised in aqueous alkaline solution, and 3 : 4-dimethylcatechol gives a deep, reddish-brown, rather than the typical red colour, under the same conditions.

A major advance was reported by Bristow in 1947 (*J. Inst. Fuel*, 1947, **20**, 109), namely, that the red colour was produced only by the simultaneous oxidation in alkaline solution of a homocatechol and derivatives of resorcinol (see also Low Temperature Carbonisation Limited, Bolsover, Chesterfield, B.P. 621,639/1949). It was later found (Baker *et al.*, *loc. cit.*) that for the production of the typical red colour the catechol must have a methyl group in a position *para* to one or other of the hydroxyl groups, but that the nature of the resorcinol was not critical. The introduction of further nuclear methyl groups into either the catechol or the resorcinol was found to change the colour from orange to bright red, and the most brilliant red colour was given by a mixture of 3 : 5-dimethylcatechol and 2 : 4-dimethylresorcinol. In the light of these facts it seems probable that the material separated by Burke and Caplan contained 3 : 5- and 3 : 6-dimethylcatechol and small quantities of 2-methyl-, 4-methyl-, and 2 : 4-dimethyl-resorcinol which would be in part extracted with the catechols; all these compounds are known to occur in low-temperature coal tar.

At the outset of the present investigation, it was clear that the red colouring matters were the alkali salts of hydroxylated quinonoid compounds. The red solutions become yellow or orange on the addition of acid, and colourless on reduction in presence of either alkali or acid. It was also evident that oxidative coupling occurred between the catechol and the resorcinol, followed by further oxidation to a quinone.

It was decided to investigate in detail the oxidative coupling of 3 : 5-dimethylcatechol (I) with 2 : 4-dimethylresorcinol (II), because the chances of obtaining a single product from what otherwise would certainly be a complex reaction mixture, were expected to be greatly improved by restricting the number of reactive nuclear positions at which coupling or oxidation might occur, and in conformity with this it was found that reaction between the two components (I) and (II) was unique in that it readily yielded a well-crystalline product. 2 : 4-Dimethylresorcinol (II) is reactive only at position 6, and reaction in 3 : 5-dimethylcatechol (I) is restricted to positions 4 and 6, and analogy suggests that position 4 is likely to be the more reactive. No trialkylcatechol was available.



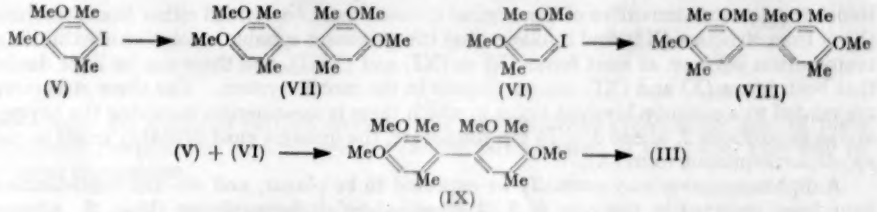
When air was drawn through a solution of equal quantities of 3 : 5-dimethylcatechol (I) and 2 : 4-dimethylresorcinol (II) in 1% aqueous sodium hydroxide containing sodium carbonate, a dark magenta, crystalline solid slowly separated from the intensely red solution. This solid, which was produced in extremely high yield, is the monosodium salt, probably hydrated, of the bright orange parent substance, $C_{16}H_{16}O_4$, which yielded a yellow, crystalline diacetyl derivative, $C_{16}H_{14}O_2(OAc)_2$. The substance $C_{16}H_{16}O_4$ was reduced by sodium dithionite in alkaline solution, and by zinc dust in acetic acid; catalytic reduction resulted in the uptake of one mol. of hydrogen. These reduced solutions when alkaline were rapidly reoxidised by air to give the original colouring matter, and attempts to effect methylation or acetylation of this presumed tetrahydroxy-compound gave uncrystallisable products. The evidence suggested that the red colouring matter was the monosodium salt of a quinone derived from a dihydroxy-tetramethyl-diphenyl; the possibility that the compound might be a quinone of the type $O{:}C_6H_4{:}CH{\cdot}CH{:}C_6H_4{:}O$ (see Yohe, Hill, Dunbar, and Scheidt, *J. Amer. Chem. Soc.*, 1953, **75**, 2688) was excluded by the elementary analysis, by the absorption of only one mol. of hydrogen on catalytic reduction, and by synthetical evidence described below.

The sodium salt of the quinone is intensely coloured: one part in 10^5, 10^6, and 10^7 parts of water gives bright red, pink, and just discernibly pink solutions respectively. The substance is an indicator, changing from red to yellow over the pH range 7·3—5·2, and it dyes silk and wool (see Experimental section).

The reaction in the production of the colouring matter must be, first, oxidative coupling to give a tetrahydroxydiphenyl derivative (III), or rather less probably (IV), and, secondly,

removal of two atoms of hydrogen to form a quinone. Confirmation of the structure (III) of the parent tetrahydroxy-compound was obtained by synthesis in the following way.

3 : 5-Dimethylcatechol (I) and 2 : 4-dimethylresorcinol (II) were each dimethylated, and the dimethyl ethers treated with iodine and mercuric oxide in boiling ethanol, yielding 4-iodo-3 : 5-dimethylveratrole (V) and 1-iodo-2 : 4-dimethoxy-3 : 5-dimethylbenzene (VI) respectively. Proof of the position of the iodine atom in (V) is given later. Ullmann coupling reactions were then carried out on each of these iodo-compounds separately, and on a mixture of the two. Compound (V) gave 3 : 4 : 3′ : 4′-tetramethoxy-2 : 6 : 2′ : 6′-tetramethyldiphenyl (VII), m. p. 173°, and compound (VI) gave 2 : 4 : 2′ : 4′-tetramethoxy-3 : 5 : 3′ : 5′-tetramethyldiphenyl (VIII), m. p. 107°. The mixed Ullmann reaction with both (V) and (VI) gave a mixture of the two solid, symmetrical diphenyls (VII) and (VIII) which are both very sparingly soluble in ether, and the liquid, asymmetrical 2 : 4 : 3′ : 4′-tetramethoxy-3 : 5 : 2′ : 6′-tetramethyldiphenyl (IX) which is totally miscible with ether.

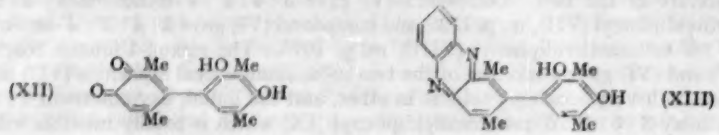


The asymmetrical diphenyl (IX) was demethylated with hydrobromic acid in acetic acid, and the resulting 2 : 4 : 3′ : 4′-tetrahydroxy-3 : 5 : 2′ : 6′-tetramethyldiphenyl (III) was oxidised under the same alkaline conditions as were used in the oxidative coupling of 3 : 5-dimethylcatechol (I) with 2 : 4-dimethylresorcinol (II). The behaviour of this tetrahydroxytetramethyl-diphenyl (III) was exactly the same as that of the mixture of (I) and (II), and the resulting crystalline sodium salt gave the orange quinonoid compound in 93·5% yield from (IX); this was identical in all respects, including the melting-point of the diacetyl derivative, with the compound prepared previously. The very high yield of the quinone from (IX) shows that (IX), although not crystalline, could not have contained more than traces of the two solid symmetrical diphenyls (VII) and (VIII), and proves the orientation of the oxygen atoms and methyl groups in the final quinone. It may be added that similar demethylation and alkaline oxidation of the two diphenyls (VII) and (VIII) gave dark brownish solutions which when acidified deposited only traces of flocculent materials.

The structure of the orange quinone derived from (III) by removal of two atoms of hydrogen is not easy to determine, and the evidence cited below proves that in solution it exhibits prototropic tautomerism. Three quinonoid structures may be derived from the tetrahydroxy-compound (III): the *pp*′-diphenoquinone (X), the *op*′-diphenoquinone (XI),

and the *o*-benzoquinone (XII). In all these structures the oxygen atom in position 4′ of the catechol nucleus is in the carbonyl form. Considered as individual substances, (X) would appear to be the most probable, as many stable *pp*′-diphenoquinones have been prepared. *op*′-Diphenoquinones corresponding to (XI) are not known, and the *o*-benzoquinone (XII) appears unlikely in view of the known instability of these compounds, and the fact that *o*-quinones cannot usually be prepared by aerial oxidation of catechols in alkaline solution. Nevertheless, the quinone can react as (XII) because it gives a quinoxaline derivative (XIII) in high yield when treated with *o*-phenylenediamine in glacial acetic acid; this quinoxaline gives a diacetyl derivative. When, however, the diacetyl derivative of the original quinone was condensed with *o*-phenylenediamine under the same

conditions it gave a quinoxaline in small yield, which proved to be a *mono*acetyl derivative of (XIII), acetylation of which gave the diacetyl derivative of (XIII) previously prepared. Moreover, when the diacetyl derivative of the quinone was treated with *o*-phenylenediamine under completely anhydrous conditions, no reaction occurred, so that it cannot be derived from the *o*-benzoquinone structure (XII). Therefore the formation of a monoacetylated quinoxaline as described above is due to partial deacetylation of the acetoxyl group in position 3 of the catechol nucleus, thus permitting the formation of an *o*-quinonoid grouping.



Hence the diacetyl derivative of the original quinone must be derived either from structure (X) or from structure (XI), and it follows that the quinone is capable in solution of exhibiting tautomerism between at least forms (X) or (XI) and (XIII), and there can be little doubt that both forms (X) and (XI) can participate in the mobile system. The three structures are related to a common bivalent anion in which there is mesomerism involving the oxygen atoms in positions 2, 4, and 3′. In the solid state, the quinone most probably exists in the *pp*′-diphenoquinone form (X).

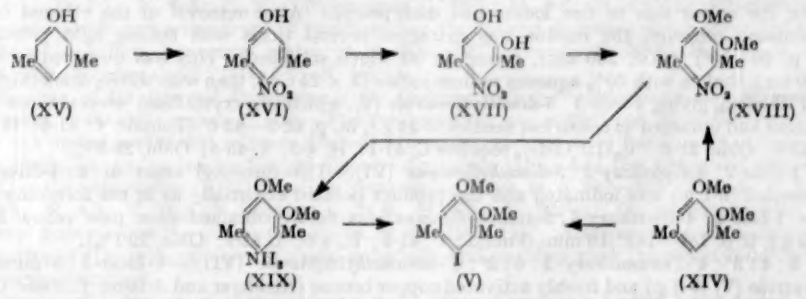
A diphenoquinone may normally be expected to be planar, and *cis*- and *trans*-isomers have been reported in the case of 3 : 3′-dimethyl-*pp*′-diphenoquinone (Moir, *S. African J. Sci.*, 1911, **8**, 253). Planar *cis*- and *trans*-forms are most unlikely in the case of the quinonoid structures (X) and (XI) owing to steric interference between the hydroxyl or carbonyl group in position 2 and the methyl groups in positions 2′ and 6′. This interference can be avoided by twisting, through a considerable angle (probably not less than 45°), and perhaps bending the molecule about the central bond, but this can only be done with loss of resonance energy and the assumption of enantiomorphous conformations. Nevertheless, that some degree of conjugation occurs between the two rings is proved by the occurrence of forms (X) or (XI) (or both) and by the very marked change of colour and in intensity of colour when the free quinone is converted into its sodium salt. The fact that the quinone reacts readily and even unexpectedly in the *o*-benzoquinonoid form (XII) may perhaps be attributed to the fact that in this form there is minimum steric interference.

Whatever may be the precise structure and conformation of the quinone, the hydroxyl group in position 2 will be sterically hindered, and this may in part account for the failure to obtain a homogeneous dimethyl ether of the quinone. Steric hindrance will also affect the reactivity of the hydroxyl group in position 2 of the related 2 : 4 : 3′ : 4′-tetrahydroxy-3 : 5 : 2′ : 6′-tetramethyldiphenyl (III) from which homogeneous tetramethyl and tetraacetyl derivatives could not be obtained.

The quinone has a very well-defined absorption maximum at 434 mμ, and two lower maxima at shorter wavelengths. The same type of curve is shown by *pp*′-diphenoquinone which has its main maximum at 398 mμ (Brown and Todd, *J.*, 1954, 1282), and by 3 : 5 : 3′ : 5′-tetramethyl-, -tetra-*tert.*-butyl-, and -tetrachloro-*pp*′-diphenoquinone which exhibit strong maxima at 414, 420, and 435 mμ respectively.

The structure, that of 4-iodo-3 : 5-dimethylveratrole (V), assigned to the product obtained by the direct iodination of 3 : 5-dimethylveratrole (XIV) was established by independent synthesis. 3 : 5-Dimethylphenol (XV) was nitrated, and the steam-involatile *p*-nitrophenol derivative (XVI) separated from the mixture of isomerides. Application of the Elbs persulphate oxidation to (XVI) gave 3 : 5-dimethyl-4-nitrocatechol (XVII), which when methylated gave 3 : 5-dimethyl-4-nitroveratrole (XVIII), a product which was identical with that prepared by the direct nitration of 3 : 5-dimethylveratrole (XIV). Reduction of the nitro-compound (XVIII) gave 4-amino-3 : 5-dimethylveratrole (XIX), which was converted into 4-iodo-3 : 5-dimethylveratrole (V) *via* the diazonium salt. This iodo-compound was identical with the direct iodination product of 3 : 5-dimethylveratrole (XIV). The orientation disclosed is that expected in a derivative of veratrole.

The salt of the quinone described in this paper is certainly not the only colouring matter formed by the alkaline oxidation of phenols from low-temperature carbonisation and other coal tars. Catechols in general give brownish solutions in alkalis, and virtually any mixture of a catechol with a resorcinol gives some kind of red-brown or red colour. From the present work it seems likely that the compounds which contribute to the more purely



red colours are quinones derived from 2 : 4 : 3′ : 4′-tetrahydroxydiphenyls, and of these substances the intensely coloured and very stable salt described in this paper may well be of major importance.

Experimental

Reaction between 3 : 5-Dimethylcatechol and 2 : 4-Dimethylresorcinol.—3 : 5-Dimethylcatechol (I) (5·0 g.) and 2 : 4-dimethylresorcinol (II) (5·0 g.) were dissolved in 1% aqueous sodium hydroxide (200 c.c.) containing anhydrous sodium carbonate (19·5 g.), and air was aspirated through the solution for 14 hr. The red colour became progressively darker, and the magenta, crystalline *salt* which slowly separated was collected, washed with a little ice-cold water, and dried (yield 12·1 g.) (Found in material dried at 100°/0·1 mm.: Na, 7·4. $C_{16}H_{15}O_4Na$ requires Na, 7·8%). This salt was suspended in water (100 c.c.) and acidified with hydrochloric acid, and the orange precipitate collected, washed, and crystallised several times from hot methanol, giving the *quinone* as orange needles (*ca.* 9·0 g.), m. p. 227—228° (decomp.) (Found: C, 70·6; H, 5·9. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%). If the sodium carbonate is omitted in the preparation, the sodium salt of the quinone is not precipitated and the free quinone may be obtained by acidification; after one crystallisation from methanol, the yield is 92% (9·10 g.).

The quinone dyes silk and wool, the colours being red in alkali and yellow in acid. On wool mordanted with iron, aluminium, and chromium the colours are red-brown, orange, and brown respectively, and on similarly mordanted silk, the colours are orange, yellow-orange, and bronze-orange respectively; the colours are not greatly changed by alteration of pH. It does not dye cotton or mordanted cotton.

The *diacetyl* derivative was prepared from the quinone (0·5 g.) by suspension in acetic anhydride (10 c.c.) and treatment with pyridine (3 drops), and after ½ hr. the solution was heated on the water-bath for 2 hr. and poured into water. The precipitated oil, which solidified, was dissolved in ether, the ethereal solution washed with water and aqueous sodium hydrogen carbonate, and, after removal of the ether, the solid was crystallised several times from methanol, giving lemon-yellow needles (0·62 g.), m. p. 143—144·5° (Found: C, 67·3; H, 5·5. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·6%). An acetyl determination gave the unexpectedly high figure of 34·6% [$C_{16}H_{14}O_2(OAc)_2$ requires Ac, 24·2%], but it was found that the parent dihydroxyquinone itself gave an apparent acetyl value of 12·1% which must be due to breakdown of the molecule with formation of a volatile acid, possibly acetic acid. Hence the diacetyl derivative will give an acetyl value which is fictitiously 9·2% too high, thus bringing the value of the genuine acetyl groups to 25·4%.

3 : 5-*Dimethylveratrole.*—3 : 5-Dimethylcatechol (10 g.) in anhydrous acetone (120 c.c.) and benzene (80 c.c.) was boiled under reflux for 3 hr. with anhydrous potassium carbonate (40 g.) and methyl sulphate (10 c.c.). Further similar quantities of potassium carbonate and methyl sulphate were then added, boiling continued for 16 hr., and the filtered solution distilled, giving 3 : 5-*dimethylveratrole* as a colourless oil (11·2 g.), b. p. 118°/16 mm. [Found: C, 72·4; H, 8·6; OMe, 37·6. $C_8H_8(OMe)_2$ requires C, 72·3; H, 8·4; OMe, 37·3%].

Dimethyl Ether of **2 : 4-***Dimethylresorcinol.*—This was prepared from 2 : 4-dimethylresorcinol (10 g.) as in the case of the preceding compound. The *dimethyl ether* was obtained as a very pale yellow oil (11·0 g.), b. p. 114—115°/20 mm. (Found: C, 71·7; H, 7·9; OMe, 35·8%).

4-Iodo-3 : 5-dimethylveratrole (V).—3 : 5-Dimethylveratrole (4·07 g., 1 mol.) in ethanol (15 c.c.) was stirred under reflux on a boiling-water bath, and iodine (12·5 g., 2 mols.) and mercuric oxide (10·5 g., 2 mols.) were added in small portions during 3 hr., fresh additions being made only when the colour due to free iodine had disappeared. After removal of the ethanol under diminished pressure, the residue was extracted several times with boiling light petroleum (b. p. 60—80°) (total, 200 c.c.), giving an oil which solidified. This was dissolved in ether (100 c.c.), shaken with 20% aqueous sodium iodide (3 × 25 c.c.), then with water, dried ($MgSO_4$), and distilled, giving *4-iodo-3 : 5-dimethylveratrole* (V), which was crystallised several times from ethanol and obtained as colourless needles (5·34 g.), m. p. 62·5—63·0° [Found: C, 41·6; H, 4·8; I, 43·6; OMe, 21·5. $C_8H_7I(OMe)_2$ requires C, 41·1; H, 4·5; I, 43·5; OMe, 21·2%].

1-Iodo-2 : 4-dimethoxy-3 : 5-dimethylbenzene (VI).—The dimethyl ether of 2 : 4-dimethylresorcinol (6·1 g.) was iodinated and the product isolated essentially as in the foregoing case. The *1-iodo-2 : 4-dimethoxy-3 : 5-dimethylbenzene* was finally obtained as a pale yellow liquid (7·5 g.), b. p. 159—161°/16 mm. (Found: C, 41·9; H, 4·6; I, 42·7; OMe, 22·1%).

3 : 4 : 3′ : 4′-Tetramethoxy-2 : 6 : 2′ : 6′-tetramethyldiphenyl (VII).—4-Iodo-3 : 5-dimethylveratrole (V) (3·0 g.) and freshly activated copper bronze (Kleiderer and Adams, *J. Amer. Chem. Soc.*, 1933, **55**, 4219) (3·0 g.) were heated in a metal-bath at 220° for 2 hr. with occasional stirring. The product was extracted with hot methanol (3 × 30 c.c.), filtered, boiled with charcoal, cooled, collected, and crystallised several times from this solvent. *3 : 4 : 3′ : 4′-Tetramethoxy-2 : 6 : 2′ : 6′-tetramethyldiphenyl* was obtained as flat rhombs (1·07 g.), m. p. 172·5—173° [Found: C, 72·7; H, 7·6; OMe, 38·2. $C_{16}H_{14}(OMe)_4$ requires C, 72·7; H, 7·9; OMe, 37·6%].

2 : 4 : 2′ : 4′-Tetramethoxy-3 : 5 : 3′ : 5′-tetramethyldiphenyl (VIII).—The Ullmann reaction was carried out as in the preceding case, but with 1-iodo-2 : 4-dimethoxy-3 : 5-dimethylbenzene (VI) (5 g.). The extraction was effected with ethyl acetate, and the product crystallised several times from methanol, giving *2 : 4 : 2′ : 4′-tetramethoxy-3 : 5 : 3′ : 5′-tetramethyldiphenyl* (VIII) (2·44 g.), as colourless plates, m. p. 107—108° (Found: C, 72·8; H, 7·8; OMe, 38·7%).

Ullmann Reaction on a Mixture of **4-***Iodo-3 : 5-dimethylveratrole* (V) *and* **1-***Iodo-2 : 4-dimethoxy-3 : 5-dimethylbenzene* (VI). *Formation of* **2 : 4 : 3′ : 4′-***Tetramethoxy-3 : 5 : 2′ : 6′-tetramethyldiphenyl* (IX).—The two iodo-compounds (V) and (VI) (4·705 g. each) were mixed by melting, freshly activated copper bronze (9·41 g.) was added, and the mixture heated in a metal-bath at 190—200° for 6 hr. with occasional stirring. The product was then extracted with hot ethyl acetate (4 × 50 c.c.), giving a brown oil (5·93 g.) which was subjected to steam-distillation to remove unchanged iodo-compounds. The steam-distillate (total, 2200 c.c.) yielded first unchanged (VI) (1·55 g.), then unchanged (V) (1·2 g.), then an oil (0·51 g.), and finally a very sparingly volatile, halogen-free oil (0·04 g.), presumably a mixture of the three diphenyls (VII), (VIII), and (IX). To the residual, viscous oil (2·56 g.), which was also halogen-free, was added a little ether. A crystalline solid separated and this was collected; the ethereal solution was evaporated and treated with ether as before, again giving a little solid material. This process was repeated 8 times, whereafter no more crystals were obtained; fractional crystallisation of these united products gave the symmetrical diphenyls (VII) (0·59 g.) and (VIII) (0·78 g.). The final non-crystalline product (1·145 g.) was steam-distilled, and the distillate (8 l.) extracted with ether, giving a colourless oil (0·81 g.) which was distilled in a micro-still at 85°/0·1 mm. This *2 : 4 : 3′ : 4′-tetramethoxy-3 : 5 : 2′ : 6′-tetramethyldiphenyl* (IX) could not be obtained crystalline (Found: C, 72·7; H, 7·7; OMe, 37·8%).

Demethylation and Subsequent Alkaline Oxidation of **2 : 4 : 3′ : 4′-***Tetramethoxy-3 : 5 : 2′ : 6′-tetramethyldiphenyl* (IX).—The diphenyl (IX) (0·47 g.) was boiled under reflux with acetic acid (7 c.c.) and 50% aqueous hydrobromic acid (7 c.c.) for 6 hr., water (200 c.c.) added, the product extracted with ether (3 × 75 c.c.), dried, distilled, and the residue boiled in methanol with charcoal and recovered, giving a light-brown resin (0·334 g.) which did not crystallise. This product is undoubtedly essentially 2 : 4 : 3′ : 4′-tetrahydroxy-3 : 5 : 2′ : 6′-tetramethyldiphenyl (III).

The resinous material (0·334 g.) was dissolved in 1% aqueous sodium hydroxide half saturated with sodium carbonate (5·5 c.c.), and air was drawn through the solution for 1½ hr. The precipitated magenta solid was separated by centrifugation, washed once with a little ice-cold water, suspended in water (15 c.c.), and acidified with hydrochloric acid. The precipitate crystallised from methanol (charcoal) as orange needles (0·31 g.), m. p. 227—228° (decomp.) undepressed on admixture with the specimen of the quinone previously described (Found: C, 70·2; H, 6·0. Calc. for $C_{14}H_{14}O_4$: C, 70·6; H, 5·9%). The identity of the two specimens

was further confirmed by converting the new material into the diacetyl derivative as previously described; it formed lemon-yellow needles, m. p. and mixed m. p. 143—144·5°.

Reaction of the Quinone with o-*Phenylenediamine. Formation of the Quinoxaline* (XIII).—The quinone (2·29 g., 1 mol.) and *o*-phenylenediamine (1·1 g., 1·2 mols.) were heated to boiling in glacial acetic acid (50 c.c.), then cooled, and the yellow solid was collected, washed, and crystallised from methanol, giving yellow needles (2·56 g., 88·5%), m. p. 194—195° (Found: C, 76·3; H, 5·7; N, 8·2. $C_{22}H_{20}O_3N_2$ requires C, 76·7; H, 5·8; N, 8·1%). Reaction with acetic anhydride and a few drops of pyridine gave the *diacetyl derivative* which separated from methanol in yellow, hexagonal plates, m. p. 206—207° (Found: C, 72·6; H, 5·6; N, 6·6. $C_{26}H_{24}O_4N_2$ requires C, 72·7; H, 5·6; N, 6·5%).

Reaction of the Diacetyl Derivative of the Quinone with o-*Phenylenediamine. Monoacetyl Derivative of the Quinoxaline* (XIII).—The condensation was carried out as in the preceding case, the cooled acetic acid solution diluted with water, and the solid fractionally crystallised from methanol, giving the unchanged diacetyl derivative (84%) and the *monoacetyl derivative* (11%) of the quinoxaline (XIII) as yellow, rectangular plates, m. p. 207—208° (Found: C, 74·4; H, 5·8; N, 6·9. $C_{24}H_{22}O_3N_2$ requires C, 74·6; H, 5·7; N, 7·2%). On admixture with the diacetyl derivative of the quinoxaline the m. p. was 190—195° Acetylation of the monoacetyl derivative of the quinoxaline with acetic anhydride and pyridine gave the diacetyl derivative previously described.

The diacetyl derivative of the quinone was recovered unchanged after being boiled with *o*-phenylenediamine in benzene for 3 hr., anhydrous ethanol for 4 hr., or acetic acid and a trace of acetic anhydride for 4 hr.

1 : 3-*Dimethoxy*-2 : 4-*dimethyl*-6-*nitrobenzene*.—The dimethyl ether of 2 : 4-dimethylresorcinol (8·25 g.) was dissolved in acetic acid (80 c.c.) and concentrated nitric acid (4·5 c.c.) added. Next day the solution was poured into water (500 c.c.) and extracted with ether, the extracts were steam-distilled, and the product was again taken up in ether and finally distilled, giving 1 : 3-*dimethoxy*-2 : 4-*dimethyl*-6-*nitrobenzene* as a light yellow oil (5·0 g.), b. p. 110—112°/0·3 mm. (Found: C, 56·9; H, 6·1; N, 6·9. $C_{10}H_{13}O_4N$ requires C, 56·9; H, 6·2; N, 6·6%).

3 : 5-*Dimethyl*-4-*nitrophenol* (XVI).—The mononitration of 3 : 5-dimethylphenol was carried out as described by Adams and Stewart (*J. Amer. Chem. Soc.*, 1941, **63**, 2861), but the tedious removal of the *o*-nitrophenol derivative, 3 : 5-dimethyl-2-nitrophenol, by steam-distillation was in part avoided by several preliminary extractions with cold light petroleum in which the required *p*-nitrophenol derivative, 3 : 5-dimethyl-4-nitrophenol (XVI), is very sparingly soluble. Crystallisation of (XVI), m. p. 107—108°, is conveniently effected from hot, very dilute hydrochloric acid.

3 : 5-*Dimethyl*-4-*nitrocatechol* (XVII).—To a stirred solution of 3 : 5-dimethyl-4-nitrophenol XVI) (25 g., 1 mol.) in water (900 c.c.) containing sodium hydroxide (30 g.) was added finely powdered potassium persulphate (40·5 g., 1 mol.) during 3 hr. After being kept for 48 hr., the red solution was acidified with dilute dihydrochloric acid (Congo-red), precipitating unchanged 3 : 5-dimethyl-4-nitrophenol (11·2 g.) of which a further quantity (3·7 g.) was obtained by extracting the filtrate with ether. To the aqueous solution was now added an excess of concentrated hydrochloric acid, the mixture boiled for ½ hr. to hydrolyse the phenyl sulphate group, cooled, and extracted with ether (5 × 100 c.c.), and the recovered product crystallised from methanol (charcoal) and then from water. 3 : 5-*Dimethyl*-4-*nitrocatechol* (8·7 g.) was obtained as thick, yellow plates, m. p. 124—125° (Found: C, 52·3; H, 4·9; N, 7·3. $C_8H_9O_4N$ requires C, 52·5; H, 4·9; N, 7·7%). When kept under anhydrous conditions it becomes dark brown. Its alcoholic solution becomes emerald-green on addition of a trace of ferric chloride. The *dibenzoyl* derivative forms colourless needles, m. p. 87—88°, from ethanol (Found: C, 67·7; H, 4·3; N, 3·8. $C_{23}H_{17}O_6N$ requires C, 67·5; H, 4·3; N, 3·6%).

3 : 5-*Dimethyl*-4-*nitroveratrole* (XVIII).—(a) *Nitration of* 3 : 5-*dimethylveratrole*. 3 : 5-Dimethylveratrole (11·3 g.) was dissolved in glacial acetic acid (55 c.c.) and concentrated nitric acid (12·5 c.c.) added. Next day the solution was poured into water, and after cooling to 0° the yellow solid was collected, washed, and crystallised several times from light petroleum (b. p. 60—80°) (yield 3·1 g.). 3 : 5-*Dimethyl*-4-*nitroveratrole* forms pale yellow needles, m. p. 86—86·5° [Found: C, 57·0; H, 6·2; N, 6·6; OMe, 29·8. $C_8H_7C_2N(OMe)_3$ requires C, 56·9; H, 6·2; N, 6·6; OMe, 29·4%].

(b) *Methylation of* 3 : 5-*dimethyl*-4-*nitrocatechol*. To 3 : 5-dimethyl-4-nitrocatechol (XVII) (3·65 g.) in ethanol (50 c.c.) were added alternately (½ hr.) in portions, with shaking in an atmosphere of nitrogen, methyl sulphate (38·4 c.c.) and a concentrated solution of potassium hydroxide in water (50% w/w) (51 g.). The temperature was kept at about 50°. The ethanol

was then removed under diminished pressure, the mixture heated on the water-bath for ½ hr., water added, and the solid collected and crystallised from light petroleum (charcoal), giving **3 : 5-dimethyl-4-nitroveratrole** (3·0 g.), m. p. and mixed m. p. 86—87°.

4-Amino-3 : 5-dimethylveratrole (XIX).—**3 : 5-Dimethyl-4-nitroveratrole** (0·43 g.) was catalytically reduced in ethyl acetate (100 c.c.) in presence of Raney nickel (*ca.* 0·5 g.) at 3 atm. Filtration and removal of the solvent gave the crude amino-compound as a readily oxidisable, light brown oil which solidified at 0°. The *N-benzoyl* derivative, prepared by reaction with benzoyl chloride in pyridine, separated from 50% ethanol in minute plates, m. p. 169·5—170·5° [Found: C, 71·7; H, 6·5; N, 5·2; OMe 21·2. $C_{15}H_{15}ON(OMe)_3$ requires C, 71·6; H, 6·7; N, 4·9; OMe, 21·8%].

4-Iodo-3 : 5-dimethylveratrole (V) *from 4-Amino-3 : 5-dimethylveratrole* (XIX).—Crude 4-amino-3 : 5-dimethylveratrole (above) (0·5 g.) was dissolved in concentrated sulphuric acid (0·4 c.c.), diluted with water (3·3 c.c.), and diazotised at 0° by the addition of sodium nitrite (0·2 g.) in water (2·0 c.c.). The excess of nitrous acid was destroyed by urea, sodium iodide (0·63 g.)

Ultraviolet absorption characteristics of the quinone, $C_{16}H_{16}O_4$, *in ethanol.*

$\lambda_{max.}$ (mμ)	$\log_{10}\varepsilon$	$\lambda_{min.}$ (mμ)	$\log_{10}\varepsilon$
434·0	4·19	322·0	3·68
303·5	3·71	275·0	3·50
258·6	3·80	248·0	3·74

in water (2 c.c.) added, and the solution stirred for 1 hr., kept for 4 hr., heated on the steam-bath for 2 hr., and steam-distilled. The distillate yielded to ether a solid which after crystallisation from ethanol (charcoal) formed needles (0·62 g.), m. p. 62·5—63°, undepressed when mixed with the specimen of 4-iodo-3 : 5-dimethylveratrole previously prepared.

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Immunopolysaccharides. Part V. Structure of a Modified* Betacoccus arabinosaceous *Dextran.*

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A polyglucosan, elaborated when *Betacoccus arabinosaceous* (Birmingham strain) is grown in a magnesium-deficient medium, is shown to be a dextran, in which the principal glucosidic linkages are α-1 : 6, a small proportion of the glucose residues being involved in branching of the 1 : 3-type. The average chain-length is 40—50 units.

IT has been proved (Barker, Bourne, Bruce, and Stacey, *Chem. and Ind.*, 1952, 1156; Barker, Bourne, Bruce, Neely, and Stacey, *J.*, 1954, 2395) that *Betacoccus arabinosaceous* (Birmingham strain) normally produces a highly branched dextran (average chain-length, 6—7 glucose residues), in which the branch points involve positions 1 and 3. However, in the autumn of 1951, one of us (A. E. J.) isolated samples of dextran in an unusual granular form during commercial production of the polysaccharide, using the same organism. It is one of these samples which is the subject of the present communication.

The organism, which appeared to have the usual culture characteristics (Stacey and Swift, *J.*, 1948, 1555), was grown on an 800-gallon scale in a yeast–sucrose–phosphate stock medium. Formation of the granular dextran introduced difficulties in the operation of the plant, which made a detailed structural study desirable. In addition, the phenomenon was of considerable biochemical interest because it was later established that it arose through magnesium deficiency, caused by removal of a magnesium-rich precipitate during the preparation of the sterile medium. The ability of the organism to produce the usual

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highly branched dextran was regained when it was subsequently cultured on magnesium-rich media.

The dextran, which was virtually free from lower saccharides, minerals, and nitrogenous materials, had $[\alpha]_D^{19}$ +194° in N-sodium hydroxide, compared with +202° for the normal highly branched dextran (Barker *et al.*, *loc. cit.*, 1954). These values are consistent with Jeanes and Wilham's observation (*J. Amer. Chem. Soc.*, 1952, **74**, 5339) that dextrans with smaller proportions of 1 : 3-linkages have lower rotations. Paper-chromatographic analysis of a hydrolysate showed only glucose, which was later crystallized; the extent of the conversion was shown by cuprimetric titration to be 97%.

The dextran was methylated with sodium hydroxide and methyl sulphate, by a procedure similar to that employed by Peat, Schlüchterer, and Stacey (*J.*, 1939, 581). The product had OMe, 45·2% (a tri-*O*-methylglucosan requires OMe, 45·6%). A paper chromatogram of a hydrolysate of the trimethyl ether revealed three components, having R_P values and staining properties identical with those of 2 : 3 : 4 : 6-tetra-*O*-methyl-, 2 : 3 : 4-tri-*O*-methyl-, and 2 : 4-di-*O*-methyl-glucose, respectively.

The identity of the methylglucoses was confirmed by fractionation of a hydrolysate of the methylated dextran on a silica gel column (Bell, *J.*, 1944, 473). The 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose was characterized as the crystalline α-anomer and as the aniline derivative, and the tri-*O*-methyl-D-glucose by conversion into 2 : 3 : 4-tri-*O*-methyl-*N*-phenyl-D-glucosylamine. The 2 : 4-di-*O*-methyl-D-glucose was present in insufficient amount for crystallization and was characterized by comparing it, chromatographically and ionophoretically, with an authentic sample (supplied by Dr. D. J. Bell) and with specimens of 2 : 3- and 3 : 4-di-*O*-methyl-D-glucose.

The mixture of saccharides produced by partial hydrolysis of the dextran was fractionated on a charcoal column (Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677). *iso*Maltose, identified as its crystalline β-octa-acetate, constituted the major portion of the disaccharide fraction, only a trace of a second disaccharide, having the R_P value of nigerose, being detected. The *iso*maltotriose fraction was not accompanied by any other detectable trisaccharide.

The dextran consumed 1·96 mol. of periodate and produced 0·94 mol. of formic acid per anhydroglucose unit, when oxidized for 112 hr. at 26°. On the assumption that only 1 : 3-branches were present, the former figure indicated a chain-length of approximately 50 glucose residues, while the latter corresponded to a chain-length of only *ca.* 17. This low value for formic acid (0·94 mol. instead of 0·98 mol.) may well be attributable to the inaccuracy of the determination in the presence of oxidized polysaccharide. The chain-length of 50 is in reasonable agreement with the value (40) calculated from the proportion of "tetra" in the hydrolysate of the methylated dextran. Again, hydrolysis of the periodate-oxidised dextran gave, *inter alia*, a component with an R_P value equal to that of glucose, in an amount estimated visually, by comparison with standards, to correspond to a chain-length of *ca.* 50 units. The appearance of this sugar confirmed the presence of 1 : 3-branch points.

Finally, the infrared absorption spectrum of the dextran was consistent with its negligible degree of branching (cf. Barker, Bourne, Stacey, and Whiffen, *J.*, 1954, 171). There were absorption peaks at 917 and 768 cm.$^{-1}$ (α-1 : 6-linkages) and at 841 cm.$^{-1}$ (shown by α-anomers in the D-glucopyranose series), no absorption at *ca.* 794 cm.$^{-1}$ (α-1 : 3-linkages) being detectable. The normal highly branched dextran produced by *Betacoccus arabinosaceous* does give an absorption band at 794 cm.$^{-1}$ (Barker *et al.*, *loc. cit.*, 1954).

Thus it is clear that the degree of branching in the dextran synthesized by this organism is dependent on the composition of the culture medium. Magnesium favours the production of branches, possibly because it is a component of the enzyme system responsible for their formation.

Experimental

Isolation of the Dextran.—*Betacoccus arabinosaceous* (Birmingham strain) was grown on a yeast–sucrose–phosphate stock medium in 800-gallon tanks for 2 days. The viscous mass was degraded at pH 7·0 and 160°, in the presence of sodium sulphite and calcium carbonate (cf.

Stacey and Pautard, *Chem. and Ind.*, 1952, 1058), until the mean molecular weight of the dextran, as determined by viscosity measurements, was 200,000. The bacterial debris was adsorbed on a calcium phosphate flock and filtered off. The dextran was precipitated several times with acetone and dried at 60° *in vacuo* over phosphoric oxide; it had ash, 0·07; N, 0·4%; $[\alpha]_D^{19}$ +194° (*c*, 1·0 in N-NaOH).

Paper chromatography of the dextran, with the upper phase of *n*-butanol–ethanol–water–ammonia (40 : 10 : 49 : 1) as the solvent, and the usual naphtharesorcinol, aniline hydrogen phthalate, and ammoniacal silver nitrate sprays, failed to reveal any oligosaccharides.

Acidic Hydrolysis of the Dextran.—The polysaccharide (20 mg.) was hydrolysed with 1·4N-sulphuric acid (2 c.c.) at 100° for 5 hr. in a sealed tube. After the removal of ions by Consden, Gordon, and Martin's method (*Biochem. J.*, 1947, **41**, 590), the neutral hydrolysate was examined by paper chromatography, as described above; the single component had an R_F value equal to that of glucose.

Another sample of the polysaccharide was hydrolysed for 5 hr. with 1·4N-sulphuric acid at 100°, and the glucose produced was determined by cuprimetric titration (Bourne, Donnison, Haworth, and Peat, *J.*, 1948, 1687). After a small correction (2%) for the loss in reducing power which occurs when glucose itself is treated with acid under these conditions (Pirt and Whelan, *J. Sci. Food Agric.*, 1951, **2**, 224), the extent of the conversion corresponded to 97%.

After hydrolysis of another sample (1·00 g.) of the dextran, during which $[\alpha]_D$ fell to +52° (constant), α-D-glucose was obtained, having m. p. and mixed m. p. 142—144°. This was further characterized as penta-*O*-acetyl-β-D-glucopyranose, m. p. and mixed m. p. 131—133°.

Methylation of the Dextran.—The dextran (8·0 g.) was dissolved in 30% sodium hydroxide solution (100 c.c.) and treated at 40—50° with methyl sulphate (180 c.c.) and 30% sodium hydroxide solution (250 c.c.), following the procedure of Peat, Schlüchterer, and Stacey (*loc. cit.*). After fifteen such methylations the crude methyl ether (5·2 g.) was purified by extraction with chloroform, concentration to a syrup, and precipitation of the methylated dextran with an excess of light petroleum. The product had ash, 0·12; OMe, 45·2% (Calc. for $C_9H_{16}O_5$: OMe, 45·6%).

Identification of the Methyl-sugars obtained from the Methylated Dextran.—The polysaccharide ether (0·152 g.), in dry chloroform (5 c.c.), was treated with 10% methanolic hydrogen chloride (5 c.c.) in a sealed tube at 100° for 6 hr., and then, after removal of the solvent, with 4% hydrochloric acid (25 c.c.) at 100° for 6 hr., the optical rotation then being constant. The resulting solution of methylglucoses was freed from ions and concentrated to a syrup. A paper chromatogram of the hydrolysate, irrigated for 24 hr. as previously described, showed three components when sprayed with aniline hydrogen phthalate (Partridge, *Nature*, 1949, **164**, 443). The components had R_F values and staining properties identical with those of 2 : 4-di-, 2 : 3 : 4-tri-, and 2 : 3 : 4 : 6-tetra-*O*-methylglucose. The di- and tetra-methyl ethers were present in only small, apparently equal, amounts.

Isolation of the Methyl-sugars obtained from the Methylated Dextran.—The methylated dextran (2·000 g.), after methanolysis and hydrolysis, gave a syrup which was freed from ions and then fractionated by Bell's method (*loc. cit.*) on a column of silica gel (Gordon, Martin, and Synge, *Biochem. J.*, 1943, **37**, 79). Three fractions (I, 0·050 g.; II, 1·801 g.; III, 0·048 g.) were obtained; paper chromatography and ionophoresis showed them to contain, respectively, 2 : 3 : 4 : 6-tetra-, 2 : 3 : 4-tri-, and 2 : 4-di-*O*-methyl-glucose.

Fraction I, crystallized from ether, gave 2 : 3 : 4 : 6-tetra-*O*-methyl-α-D-glucose (0·020 g.), m. p. and mixed m. p. 85—88°. Its infrared spectrum over the range 1400—700 $cm.^{-1}$ was identical with that of an authentic specimen. The syrup obtained by concentration of the mother-liquors, treated with aniline (0·30 c.c.) in ethanol (10 c.c.) under reflux for 2 hr., gave 2 : 3 : 4 : 6-tetra-*O*-methyl-*N*-phenyl-D-glucosylamine (0·010 g.), m. p. and mixed m. p. 133—135°. Peat, Schlüchterer, and Stacey (*loc. cit.*) reported m. p. 135—136°.

Fraction II (0·100 g.), refluxed with aniline (0·60 c.c.) in ethanol (1·00 c.c.) for 4 hr., gave crystals, which were recrystallized from ether–light petroleum (b. p. 40—60°). This material (0·041 g.) had m. p. 147—149°, not depressed on admixture with an authentic specimen of 2 : 3 : 4-tri-*O*-methyl-*N*-phenyl-D-glucosylamine. Peat, Schlüchterer, and Stacey (*loc. cit.*) gave m. p. 145—146°.

Fraction III had R_F and M_0 values identical with those of authentic 2 : 4-di-*O*-methylglucose; it could be distinguished on the same basis from 2 : 3- and 3 : 4-di-*O*-methylglucose (cf. Barker *et al.*, *loc. cit.*, 1954).

Partial Hydrolysis of the Dextran.—The dextran (2·73 g.) was partially hydrolysed with N-sulphuric acid (100 c.c.) at 100° for 1·75 hr., $[\alpha]_D^{17}$ having then fallen to 114°. The solution was

neutralized with barium carbonate, filtered, and then fractionated on a charcoal column (Whistler and Durso, *loc. cit.*), which was washed as shown in the Table. The eluates were filtered, concentrated, freeze-dried, and then analysed by paper chromatography.

Partial acidic hydrolysis of the dextran.

Eluant	Fraction	Wt. (g.) of product	Probable sugar components (by paper chromatography)
Water, 1600 c.c.	A	0·789	Glucose
5% Ethanol (1), 1500 c.c.	B	0·256	*iso*Maltose
5% Ethanol (2), 1000 c.c.	C	trace	Nigerose
10% Ethanol, 1600 c.c.	D	0·150	Trisaccharide
15% Ethanol, 1800 c.c. ..... 35% Ethanol, 2000 c.c.	E	1·483	Higher saccharides

Fraction A was further characterized by crystallization to give α-D-glucose, m. p. and mixed m. p. 142—144°, $[\alpha]_D^{18}$ +110° ⟶ +52° (*c*, 1·02 in H_2O), and by conversion into penta-*O*-acetyl-β-D-glucopyranose, m. p. and mixed m. p. 130—132°. Fraction B had $[\alpha]_D^{20}$ + 121·8° (corrected for ash) (*c*, 0·14 in H_2O), ash 5·04%; Montgomery, Weakley, and Hilbert (*J. Amer. Chem. Soc.*, 1949, **71**, 1682) reported $[\alpha]_D^{25}$ +120° (equil.) for *iso*maltose. A portion of this product, treated with acetic anhydride and fused sodium acetate at 100° for 1 hr., gave β-*iso*maltose octa-acetate, m. p. and mixed m. p. 140—143°. Fraction D had the same R_F value as *iso*maltotriose, and, after partial hydrolysis with N-sulphuric acid for 0·5 hr. at 100°, *iso*maltotriose, *iso*maltose, and glucose were identified by paper chromatography. This trisaccharide had $[\alpha]_D^{19}$ +145° (*c*, 0·24 in H_2O), ash negligible. Jeanes, Wilham, Jones, Tsuchiya, and Rist (*J. Amer. Chem. Soc.*, 1953, **75**, 5911) reported $[\alpha]_D$ +145° for *iso*maltotriose.

Periodate Oxidation of the Dextran.—The procedure adopted was essentially that of Jeanes and Wilham (*J. Amer. Chem. Soc.*, 1950, **72**, 2655), which incorporates Fleury and Lange's method (*J. Pharm. Chim.*, 1933, **17**, 107, 196) for the determination of the quantity of periodate consumed, and that of Halsall, Hirst, and Jones (*J.*, 1947, 1427), with certain modifications, for the determination of the quantity of formic acid produced. The number of moles of sodium periodate consumed per mole of anhydroglucose was: 16·5 hr., 1·63; 22·5 hr., 1·72; 41 hr., 1·93; 112 hr., 1·96; and the corresponding figures for moles of formic acid produced were 16·5 hr., 0·76; 41 hr., 0·91; 112 hr., 0·94.

Ethylene glycol was added to destroy the excess of periodate, and sodium hydroxide to neutralize the formic acid in a solution of dextran (0·1882 g.) which had been submitted to periodate oxidation for 112 hr. under the conditions given above. The oxidized polysaccharide was obtained after dialysis and concentration under reduced pressure. After hydrolysis with 1·4N-sulphuric acid (5 c.c.) at 100° for 9 hr., the solution was neutralized with barium carbonate, filtered, and concentrated. The syrup (0·104 g.) obtained was dissolved in water (2 c.c.) and chromatographed. It showed a component having an R_F value equal to that of glucose. The amount of glucose was determined approximately by visually comparing the intensity of the spot with known standards. The amount of glucose indicated that one glucose unit in approximately every fifty of the dextran was linked through position 3.

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Cinnolines. Part XXXIV. 5-, 6-, and 7-Hydroxy- and 5-, 6-, and 7-Amino-cinnolines.*

By A. R. Osborn and K. Schofield.

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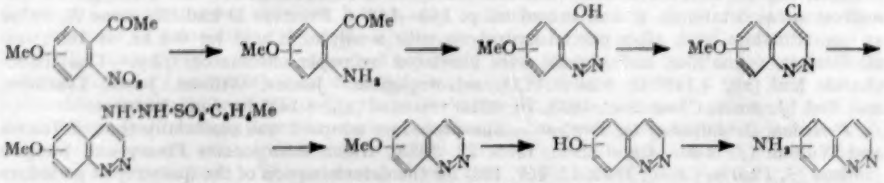
4-Hydroxy-5-, -6-, and -7-methoxycinnoline have been synthesised, and converted, through the 4-chloro-compounds into 5-, 6-, and 7-methoxycinnoline. These were demethylated to the hydroxy-compounds, which by the Bucherer reaction provided 5-, 6-, and 7-aminocinnoline.

For physical studies to be described shortly all the monohydroxy- and monoaminocinnolines were required. The 3-, 4-, and 8-isomers of both series were already known and we have now obtained the remaining members by the method used for 8-hydroxy- and 8-amino-cinnoline (Alford, Irving, Marsh, and Schofield, *J.*, 1952, 3009). The sequence of reactions involved is illustrated below, and the problem is essentially that of obtaining appropriate methoxynitroacetophenones.



The synthesis of the 5-substituted cinnolines thus required the previously unknown 2-methoxy-6-nitroacetophenone. We were unable to hydrolyse the readily available 2-methoxy-6-nitrobenzonitrile (Cartwright, Jones, and Marmion, *J.*, 1952, 3499) to the acid by the method used by Berger and Olivier (*Rec. Trav. chim.*, 1927, **46**, 600) in similarly difficult cases. However, 6-nitrosalicylic acid was obtained by Goldberg and Walker's method (*J.*, 1953, 2049) and methylation readily provided 2-methoxy-6-nitrobenzoic acid which was characterised as its methyl and ethyl esters and converted in good yield into 2-methoxy-6-nitroacetophenone by Walker and Hauser's method (*J. Amer. Chem. Soc.*, 1946, **68**, 1386).

5-Methoxy-2-nitroacetophenone was previously obtained by an inconvenient procedure by Ashley, Perkin, and Robinson (*J.*, 1930, 382) who did not record its physical properties. Whilst the nitration of *m*-hydroxybenzaldehyde gives mainly 3-hydroxy-2-nitrobenzaldehyde, *m*-hydroxybenzaldehyde "carbonate" gives 5-hydroxy-2-nitrobenzaldehyde (Mason, *J.*, 1925, 1196). *m*-Hydroxyacetophenone readily formed a "carbonate" when treated with carbonyl chloride, but nitration gave a gum from which only a small amount of 5-hydroxy-2-nitroacetophenone could be isolated. Methylation gave 5-methoxy-2-nitroacetophenone which was more practicably prepared from 5-methoxy-2-nitrobenzoic acid (Chapman, Gibson, and Mann, *J.*, 1947, 894) by the method used for the 6-isomer. Similarly, 4-methoxy-2-nitroacetophenone was obtained from 4-methoxy-2-nitrobenzoic acid (Chapman *et al.*, *loc. cit.*)

Neither 2-amino-4- nor -6-methoxybenzonitrile could be induced to react with methylmagnesium iodide or methyl-lithium, but the nitro-ketones described above were reduced to the amines, by iron and acetic acid, in good yield. The amines were converted into the 4-hydroxymethoxycinnolines by standard methods (Schofield and Simpson, *J.*, 1948, 1170). 4-Hydroxy-6-methoxycinnoline so prepared was identical with a specimen obtained earlier by the Richter reaction (Schofield and Simpson, *J.*, 1945, 512). 4-Chloro-5-, -6-, and -7-methoxycinnoline, obtained in the usual way, reacted with toluene-*p*-sulphonylhydrazide in chloroform solution to give orange-red or red products which were converted by aqueous sodium carbonate into 5-, 6-, and 7-methoxycinnoline. These were

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stable crystalline solids, in contrast to 8-methoxycinnoline which quickly liquefies and becomes green in the atmosphere (Alford *et al.*, *loc. cit.*).

Demethylation of the methoxycinnolines with hydrobromic acid gave 5-, 6-, and 7-hydroxycinnoline as crystalline solids, melting considerably higher than 8-hydroxycinnoline. Like the 8-isomer, 5-hydroxycinnoline gave a red dye with benzenediazonium chloride, but coupling was not observed with the 6- and the 7-compound. None of the hydroxy-compounds gave a noticeable colour with ferric chloride. The Bucherer reaction converted the hydroxy-compounds into the yellow, crystalline amines. 5- and 8-Aminocinnoline gave violet-red solutions in acid, 6- and 7-aminocinnoline formed yellow solutions, and all four amines formed colourless diazonium solutions which produced red dyes with alkaline β-naphthol.

Experimental

Light petroleum refers to the fraction of b. p. 40—60° unless otherwise stated.

6-Methoxy-2-nitrobenzoic Acid.—6-Nitrosalicylic acid (32·2 g.; Goldberg and Walker, *loc. cit.*), sodium hydroxide (14·1 g.), and water (90 c.c.) were stirred at 95° and treated dropwise during 1 hr. with methyl sulphate (114 g.), more 50% aqueous sodium hydroxide being added as necessary to maintain alkalinity. After 1½ hours' further heating, the mixture was cooled and acidified, and the precipitate was collected. The filtrate was extracted with chloroform, and the combined products were crystallised from water or benzene (charcoal), affording pale cream plates of 6-methoxy-2-nitrobenzoic acid (85%), m. p. 180° (Found: C, 48·7; H, 3·6. Calc. for $C_8H_7O_5N$: C, 48·7; H, 3·6%). Simonsen and Rau (*J.*, 1917, 220) gave m. p. 179—180°.

From preliminary methylations some of the *methyl ester* of the acid was isolated. It formed small colourless crystals, m. p. 62—64° (Found: C, 51·5; H, 4·0. $C_9H_9O_5N$ requires C, 51·2; H, 4·3%), from light petroleum. The *ethyl ester*, formed from the acid chloride, gave prisms, m. p. 82—83° (Found: C, 53·8; H, 5·0. $C_{10}H_{11}O_5N$ requires C, 53·3; H, 4·9%), from the same solvent.

6-Methoxy-2-nitroacetophenone.—The acid chloride [prepared in benzene from the above acid (39·4 g.) and thionyl chloride in the usual way] in the minimum amount of ether was added dropwise to a stirred ethereal solution of ethoxymagnesiomalonic ester (from 35·2 g. of ethyl malonate; Walker and Hauser, *loc. cit.*), and after being refluxed for ½ hr. the mixture was decomposed with 4N-sulphuric acid. Extraction with ether, drying ($CaSO_4$), and removal of the solvent gave an oil which was refluxed with acetic acid (60 c.c.), concentrated sulphuric acid (7·5 c.c.), and water (40 c.c.) for 4 hr. Cooling, basification, and extraction with ether yielded a sticky solid which on trituration with light petroleum provided the ketone (83%), m. p. 88°. *6-Methoxy-2-nitroacetophenone* formed cream needles, m. p. 91—92°, from light petroleum (b. p. 60—80°) (Found: C, 55·9; H, 4·8. $C_9H_9O_4N$ requires C, 55·4; H, 4·65%).

2-Amino-6-methoxyacetophenone.—The nitro-compound (32 g.) was added during 1 hr. to a stirred mixture of iron dust (46 g.), acetic acid, and water (172 c.c. of each). After being refluxed for a further hr. the mixture was cooled and extracted with ether. Evaporation and distillation gave an oil (22·43 g.), b. p. 130—160°/1·5 mm., which crystallised. *2-Amino-6-methoxyacetophenone* formed yellow cubes, m. p. 89° (Found: C, 56·1; H, 4·9, $C_9H_{11}O_2N,1·5H_2O$ requires C, 56·2; H, 7·3%) (the poor analysis is probably connected with the fact that the amine darkens quickly when kept), from ether–light petroleum. The *acetyl derivative* formed colourless needles, m. p. 124—125° (Found: C, 64·4; H, 6·4. $C_{11}H_{13}O_3N$ requires C, 63·75; H, 6·3%), from light petroleum.

4-Hydroxy-5-methoxycinnoline.—The above amine (9·9 g.) in concentrated hydrochloric acid (250 c.c.) was diazotised at 0° with sodium nitrite (5 g.) in water (10 c.c.). Concentrated hydrochloric acid (250 c.c.) was added and after four days at room temperature the solution was rapidly (15 min.) evaporated to dryness. The residue in boiling water was treated with excess of hot aqueous sodium acetate, and the precipitate was recrystallised (charcoal) from boiling water. *4-Hydroxy-5-methoxycinnoline* (5·80 g.) gave pale cream needles, m. p. 275° (decomp.) (Found: C, 60·9; H, 4·5. $C_9H_8O_2N_2$ requires C, 61·35; H, 4·6%), from water. A polymorphic form, m. p. 245° (decomp.) (Found: C, 61·2; H, 5·0%), was observed in early experiments. It changed, on standing, into the higher-melting variety.

4-Chloro-5-methoxycinnoline.—The pure hydroxycinnoline (3·4 g.) and phosphorus oxychloride (50 c.c.) were heated on the steam-bath until dissolution occurred and then for a further 3 hr. (the solution changed from green, through yellow and orange, to deep red). The cooled solution, when decomposed with ice and 4N-potassium hydroxide, yielded to ether the white

product which was used directly in the next stage. *4-Chloro-5-methoxycinnoline* gave needles, m. p. 141—142° (Found : C, 55·65; H, 3·6. $C_9H_7ON_2Cl$ requires C, 55·55; H, 3·6%), from light petroleum.

5-Methoxy-4-toluene-p-sulphonylhydrazinocinnoline Hydrochloride.—The chloro-compound, from the above preparation, in pure dry chloroform (50 c.c.) was mixed with a warm solution of toluene-*p*-sulphonylhydrazide (7 g.) in the same solvent (50 c.c.), and the whole was refluxed for 5 hr. The solvent was removed by evaporation and the orange residue used directly in the next stage. Recrystallisation from ethanol gave yellow prisms of *5-methoxy-4-toluene-p-sulphonylhydrazinocinnoline hydrochloride*, m. p. 221° (decomp.) (Found : C, 50·6; H, 4·9. $C_{16}H_{17}O_3N_4ClS$ requires C, 50·5; H, 4·5%).

5-Methoxycinnoline.—The powdered crude product above, when added during 10 min. to sodium carbonate (70 g. ; anhydrous) in water (700 c.c.) at 95°, gave an orange-red solution which was refluxed for 1 hr., cooled, and extracted with ether. Evaporation of the dried (Na_2SO_4) extract afforded the discoloured product. Three recrystallisations from light petroleum (charcoal) gave cream blades of *5-methoxycinnoline*, m. p. 92—93·5° (Found : C, 67·4; H, 5·0. $C_9H_8ON_2$ requires C, 67·5; H, 5·0%). The overall yield from 4-hydroxy-5-methoxycinnoline was 34%.

5-Hydroxycinnoline.—The pure methoxycinnoline (0·79 g.) and hydrobromic acid (50 c.c. ; *d* 1·5) were refluxed for 4 hr. The acid was removed under reduced pressure, and the yellow residue in water (25 c.c.) was brought to pH 6 with aqueous ammonia. The greenish-yellow precipitate (0·6 g.) was collected. *5-Hydroxycinnoline* gave brownish-yellow cubes, m. p. 285° (decomp.) (Found : C, 65·8; H, 4·2. $C_8H_6ON_2$ requires C, 65·75; H, 4·1%), from ethanol.

5-Aminocinnoline.—5-Hydroxycinnoline (0·26 g.), aqueous ammonia (12 c.c. ; *d* 0·88) and ammonium hydrogen sulphite (4 c.c. of a solution prepared by saturating concentrated aqueous ammonia with sulphur dioxide) were heated at 100° for 72 hr. in a sealed tube. The cooled mixture when basified with 50% aqueous potassium hydroxide yielded to chloroform a bright yellow solid (0·128 g.). *5-Aminocinnoline* formed small bright yellow prisms, m. p. 160—161° (Found : C, 65·9; H, 4·9. $C_8H_7N_3$ requires C, 66·2; H, 4·9%), after sublimation at 120°/0·1 mm. and crystallisation from benzene–*cyclo*hexane.

m-*Hydroxyacetophenone Carbonate.*—A solution of *m*-hydroxyacetophenone (13·6 g.), sodium hydroxide (4 g.), water (120 c.c.), and saturated aqueous sodium carbonate (50 c.c.) was saturated with sodium chloride. The carbonate (12·7 g. ; m. p. 75—92°) was then formed by Mason's method (*loc. cit.*), collected, washed with water, acetic acid, and again with water, and dried at 60°. The *carbonate* formed colourless plates, m. p. 98—100° (Found : C, 68·7; H, 4·7. $C_{17}H_{14}O_5$ requires C, 68·4; H, 4·7%), from ethanol.

5-Hydroxy-2-nitroacetophenone.—The carbonate (9·3 g.) and concentrated sulphuric acid (50 c.c.) were stirred at −5° and nitric acid (3·2 c.c. ; *d* 1·53) in concentrated sulphuric acid (15·5 c.c.) was added dropwise during 20 min. The deep-orange solution was stirred for a further 1 hr. at −5° and poured on ice. The orange precipitate quickly changed into a plastic solid which was washed with water and dried *in vacuo*, giving 10·9 g. of crude material. A portion of this was triturated with ethyl acetate ; the resultant brown powder, on crystallisation from this solvent, gave pale fawn needles of *5-hydroxy-2-nitroacetophenone*, m. p. 146—147° (Found : C, 54·1; H, 4·0. $C_8H_7O_4N$ requires C, 53·1; H, 3·9%).

5-Methoxy-2-nitroacetophenone.—(i) The above phenol (0·4 g.) and sodium hydroxide (0·15 g.) in water (2 c.c.) were treated at 40° with methyl sulphate (0·5 c.c.). Basification and extraction with chloroform secured the product (0·21 g.). *5-Methoxy-2-nitroacetophenone* gave colourless crystals, m. p. 69—70° (Found : C, 55·4; H, 4·6%), from benzene–light petroleum (b. p. 60—80°).

(ii) 5-Methoxy-2-nitrobenzoic acid (20 g.) was converted into the ketone (11 g.) as described for the 6-isomer, except that 1·1 equivs. of ethoxymagnesiomalonic ester were used.

2-Amino-5-methoxyacetophenone.—The above (29 g.), reduced similarly to the 6-isomer, gave a bright yellow oil (22·25 g.), b. p. *ca.* 170°/18 mm., which solidified. Recrystallised from ether–light petroleum, the *amine* formed yellow cubes, m. p. 55—55·5° (Found : C, 65·4; H, 6·5. $C_9H_{11}O_2N$ requires C, 65·4; H, 6·7%).

4-Hydroxy-6-methoxycinnoline.—Prepared from the amine (10 g.), as described for the 5-isomer, the cinnoline (5·7 g.) formed from water colourless needles, m. p. 252° (Found : C, 61·9; H, 4·8. Calc. for $C_9H_8O_2N_2$: C, 61·4; H, 4·6%), alone and with a specimen prepared by the method of Schofield and Simpson (*loc. cit.*).

6-*Methoxy-4-toluene*-p-*sulphonylhydrazinocinnoline.*—4-Chloro-6-methoxycinnoline (5·9 g. ; Keneford and Simpson, *J.*, 1947, 917), dry chloroform (200 c.c.) and toluene-*p*-sulphonylhydrazide (12 g.) were refluxed for 24 hr. and kept 1 week at room temperature. After evaporation

of the mixture to half volume the red product (10·1 g.) (probably the hydrochloride) was collected. Recrystallisation from ethanol gave cream flocks of *6-methoxy-4-toluene-p-sulphonylhydrazinocinnoline hydrate*, m. p. 199—201° (decomp.) (Found: C, 52·7; H, 4·7. $C_{16}H_{16}O_3N_4S,H_2O$ requires C, 53·0; H, 5·0%).

6-Methoxycinnoline.—The above compound (5·2 g.) was added during 10 min. to potassium carbonate (50 g.) in water (500 c.c.) at 95° and the solution was refluxed for 4 hr. Ether extracted a reddish solid which was passed in benzene over a short alumina column. The pale pink solid (1·4 g.) recovered from the eluate gave colourless needles of *6-methoxycinnoline*, m. p. 87—88° (Found: C, 59·9; H, 5·7. $C_9H_8ON_2,H_2O$ requires C, 60·7; H, 5·7%), from light petroleum.

6-Hydroxycinnoline.—Prepared from the methoxy-compound (0·20 g.) as in the 5-series, *6-hydroxycinnoline* (0·148 g.) formed cream, fluffy needles, m. p. >300° (blue-black at *ca.* 195°) (Found: C, 65·3; H, 4·2%), from water.

6-Aminocinnoline.—The hydroxy-compound (from 0·2 g. of 6-methoxycinnoline), ammonium hydrogen sulphite solution (3 c.c., prepared as before) and aqueous ammonia (10 c.c., *d* 0·88) were heated at 100° for 60 hr. in a sealed tube. Orange crystals (0·100 g.) were removed from the cooled mixture, and the filtrate was basified with 10N-potassium hydroxide and extracted with chloroform. The extract provided a solid (35 mg.) which formed bright yellow needles, m. p. 204°, when sublimed at 160°/0·5 mm. The products (0·135 g.) were combined and crystallised from benzene, giving deep yellow prisms of the *amine*, m. p. 203—204° (Found: C, 66·2; H, 5·05%).

4-Methoxy-2-nitroacetophenone.—4-Methoxy-2-nitrobenzoic acid (40 g.), by the method used for the 6-isomer, gave the *ketone* (27 g.), which formed pale yellow crystals, m. p. 49—50° (Found: C, 56·0; H, 4·6%), from ether–light petroleum.

2-Amino-4-methoxyacetophenone.—The nitro-compound (24 g.) gave in the usual way the *amine* (17·1 g.), which formed pale yellow, chunky crystals, m. p. 120—121° (Found: C, 65·6; H, 6·6%), from benzene–light petroleum (b. p. 60—80°).

4-Hydroxy-7-methoxycinnoline.—Prepared from the amine (7·9 g.) by the procedure described for the 8-isomer (Alford *et al.*, *loc. cit.*), *4-hydroxy-7-methoxycinnoline* (5·3 g.) formed needles, 255—257° (Found: C, 61·4; H, 4·6%), from water.

4-Chloro-7-methoxycinnoline.—The hydroxycinnoline (5 g.) and phosphorus oxychloride (30 c.c.) were refluxed for 2 hr. Decomposition with ice and sodium hydroxide gave a precipitate which was collected, washed with water, dried, and extracted (Soxhlet) with light petroleum. 4-Chloro-7-methoxycinnoline (5·0 g., 90%) seperated as needles, m. p. 178—179° (Found: C, 55·2; H, 3·9. $C_9H_7ON_2Cl$ requires C, 55·55; H, 3·6%).

7-Methoxy-4-toluene-p-sulphonylhydrazinocinnoline Hydrochloride.—Formed from the chlorocinnoline (13 g.) and toluene-*p*-sulphonylhydrazide (26 g.) in chloroform (1200 c.c.) after refluxing for 12 hr. and being kept for 1 week at room temperature, this *compound* (24 g.) formed small bright red crystals, m. p. 169—172° (decomp.) (Found: C, 48·2; H, 5·0. $C_{16}H_{17}O_3N_4ClS,H_2O$ requires C, 48·2; H, 4·8%), from ethanol–ether.

7-Methoxycinnoline.—The above compound (24 g.), decomposed as described for the 5-isomer, the solution being refluxed for 3 hr., yielded upon continuous ether-extraction a red solid, which was extracted (Sohxlet) with boiling light petroleum. Evaporation afforded *7-methoxycinnoline* (6·95 g.), which formed needles, m. p. 109—110° (decomp.) (Found: C, 60·4; H, 5·9; N, 16·3. $C_9H_8ON_2,H_2O$ requires C, 60·7; H, 5·7; N, 15·7%), from this solvent. Another experiment gave a product, m. p. 61—63° (decomp.) (Found: C, 62·8; H, 5·6. $C_9H_8ON_2,\frac{2}{3}H_2O$ requires C, 62·8; H, 5·5%), apparently differing in the degree of hydration.

7-Hydroxycinnoline.—The methoxy-compound (6·8 g.), demethylated as before, gave *7-hydroxycinnoline* (3·7 g.), which after crystallisation from water and then ethanol gave needles, m. p. >300° (turning blue-black at *ca.* 200°) (Found: C, 64·3; H, 4·3%).

7-Aminocinnoline.—The hydroxy-compound (0·2 g.) gave in the usual way a yellow solid (142 mg.). After sublimation (130°/0·4 mm.) and crystallisation from ethyl acetate the *amine* formed yellow needles, m. p. 191—192° (Found: C, 66·2; H, 4·9; N, 28·9. $C_8H_7N_3$ requires C, 66·1; H, 4·8; N, 29·0%).

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The Conductometric Evaluation of the Ionisation Functions of the Monohalogenoacetic Acids.

By D. J. G. Ives and J. H. Pryor.

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Conductance measurements of high accuracy on aqueous solutions of fluoro-, chloro-, bromo-, and iodo-acetic acids at 5° intervals between 15° and 35° are reported. Changes in Gibbs free energy, enthalpy, entropy, and heat capacity accompanying the dissociation of these acids have been calculated. The results are discussed in terms of the factors which determine acid strength.

Comparatively few dissociation constants of weak electrolytes have been determined as functions of temperature accurately enough for the changes in enthalpy, entropy, and heat capacity accompanying dissociation to be evaluated. All the data so far available have been obtained by the well-known E.M.F. method of Harned *et al.*, and none (except for the classical work of Schaller, *Z. physikal. Chem.*, 1898, **25**, 497) has been determined by conductance measurements. The conductance method, however, has the advantages that it approaches more closely to a purely physical method, and that it is economic of material, expeditious, and accurate. These points are illustrated in the present paper.

It is surprising that there are no satisfactory dissociation-constant data covering a range of temperatures for the four monohalogenoacetic acids, since such data would be of particular interest in studying the effects of polar substituents on acid strength. No doubt this is due to the limited availability and high toxicity of fluoroacetic acid (Saunders and Stacey, *J.*, 1948, 1773) on the one hand, and, on the other, to the tendency of the other three acids to hydrolyse, with elimination of halogen, in aqueous solution. This reaction is catalysed by silver ions and occurs rapidly at the surface of solid silver halides (Cowdrey, Hughes, and Ingold, *J.*, 1937, 1243). Use of Harned's method, involving silver–silver chloride electrodes, is therefore precluded and, very probably, an analogous method using calomel electrodes would also be unsuitable for a similar reason. It therefore seemed desirable to devise and apply a conductance method to the investigation of these acids.

It was foreseen that very accurate measurements would be necessary. The tendency to hydrolysis is enhanced in solutions of the sodium salts, and this excluded the normal procedure of obtaining ionic mobilities. Measurements on solutions of pure acids alone, therefore, had to be relied upon to provide both dissociation constants and equivalent conductances at zero concentration. All the methods designed for this purpose involve extrapolation to zero concentration and are consequently highly sensitive to systematic experimental errors. At the same time the determination of ΔH, since it is a function of the first derivative of $\ln K$ with respect to temperature, is more sensitive to errors of measurement than $\ln K$ itself. Taking these factors into account, it was judged that a limit of error of $\pm 0{\cdot}01\%$ must be set for the conductance measurements, with similarly stringent requirements for purity of materials and accuracy in the measurement of concentration and temperature.

Since the development of the conductance method to the necessary standards of accuracy forms an important part of the contribution made by the present paper, an outline is given of the essentials of the technique by which this was achieved. Whilst the main factors in the design of conductance cells and of A.C. bridges necessary to avoid systematic errors have been well understood for over 20 years, some unsatisfactory features remain, and these required special attention. Thus, although the frequency dependence of conductance measurements has been reduced to limits judged by various authors as adequate for their purposes, there is no satisfactory evidence that it has ever been entirely eliminated. Excluding gross sources of error such as the "Parker effect," the main difficulty is associated with so-called "polarisation effects" at the electrodes of the conductance cells. There can be no doubt that the essential electrical analogue of a conductance cell is a large condenser in series with an ohmic resistance, the small sinusoidal

current being carried across each interface, not by reversible ion-discharge processes, but by the very large capacity provided by the ionic double layer which resides at the interface. For high accuracy of measurement, these capacities should offer negligibly small reactance compared with the ohmic resistance of the electrolytic conductor, a condition which cannot be completely satisfied experimentally. This view is supported by the very marked effect of black platinisation of the electrodes in reducing frequency dependence; this device, however, cannot be tolerated for other reasons. The difficulty has been obviated in the present work by designing the cell shown in the Figure; this is discussed in detail in the Experimental section. It will be seen that the cell is a double one, the two parts being as nearly identical as possible, except for the distance between the electrodes, which are made from grey-platinised platinum spherical cups. All significant conductance measurements were derived from *differences* between the apparent resistances of the two parts of the cell when filled with the same solution, so that polarisation effects should be cancelled completely. Because of the difficulty of preparing two grey-platinised platinum electrodes of absolutely identical properties, this cancellation was not in fact complete, and these resistance differences retained a very small frequency dependence. The residual effect, however, seldom exceeded 0·01% within the frequency range 1150—3880 c./sec. and it was eliminated by a simple extrapolation to infinite frequency. The eminently satisfactory results of this procedure are apparent from the cell constants recorded in Table 1, in which " constants " calculated from the apparent resistances at infinite frequency of the two parts of the double cell and from the difference between these resistances are shown. Potassium chloride solutions at 25° were used for these calibrations, the extended Onsager equation (Shedlovsky, Brown, and MacInnes, *Trans. Electrochem. Soc.*, 1934, **66**, 165), with values of coefficients supplied by Gunning and Gordon (*J. Chem. Physics*, 1942, **10**,

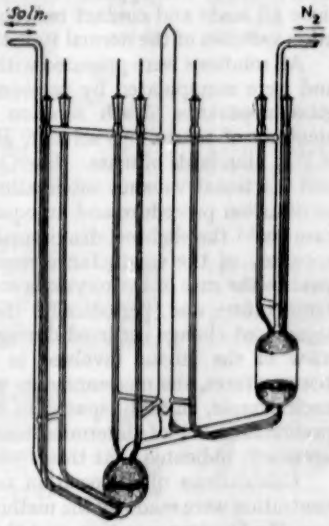

TABLE 1.

$C \times 10^4$	Λ	" Constant " of large cell	" Constant " of small cell	Ratio: large/small	Constant of double cell
106·299	141·68	0·46429	0·11680	3·9751	0·34749
74·5656	142·34	0·46422	0·11677	3·9755	0·34745
49·1596	143·04	0·46426	0·11678	3·9755	0·34748
36·6060	144·44	0·46433	0·11683	3·9744	0·34750
14·9472	146·32	0·46427	0·11683	3·9739	0·34744
13·0958	146·54	0·46430	0·11683	3·9742	0·34747
5·85475	147·62	0·46432	0·11687	3·9730	0·34745
4·31205	147·94	0·46435	0·11687	3·9732	0·34748
				Mean:	0·34747 ± 0·00002

126), being used to interpolate conductance values appropriate to the concentrations used. The equation was

$$(\Lambda + 60{\cdot}18\sqrt{C})/(1 - 0{\cdot}2289\sqrt{C}) = 149{\cdot}88 + 153{\cdot}7C + 32{\cdot}1C \log C \quad . \quad (1)$$

The final constants, over a wide range of concentrations, show a variance of only ±0·005%, with no perceptible systematic trend. Since these constants are, in effect, referred to conductance standards obtained by a high-precision direct-current method, there can be no doubt that frequency effects and all other systematic errors have been eliminated from our measurements. It can readily be shown that no significant alteration of cell constant with temperature occurred within the range of temperature used in our measurements; the cell constant also showed no change with time.

Other points relevant in characterising the method, described in detail in the Experimental section, may be mentioned. The need to set up a bridge of high precision for the conductance measurements suggested the advantage of platinum-resistance thermometry to establish the absolute temperature scale required. A thermometer for this purpose was constructed and calibrated against ice, steam, and the transition point of sodium sulphate. The readings of this thermometer were subsequently checked against N.P.L.-calibrated mercury-in-glass thermometers, with agreement consistent with errors in temperature of less than 0·002°. The "four-leads" connection system, used in modern resistance thermometry, was applied to the conductance measurements with very great advantage, since all leads and contact resistances were completely eliminated, thus allowing distribution switches of the normal type to be used for selecting cells or inserting shunts.

All solutions were prepared with water of average specific conductance $0{\cdot}1 \times 10^{-6}$ ohm^{-1} and were manipulated by pressure of highly purified nitrogen in a totally enclosed, all-glass apparatus. Each solution examined was prepared from independently weighed amounts of solute and solvent, all weighings being corrected to vacuum and to recent N.P.L. standards of mass. Each solute was rigorously purified by repeated crystallisation and fractional vacuum sublimation. Two samples were taken at different stages of the purification procedure and an equal number of solutions was prepared from each. In no case could the slightest discrimination be made between these samples within the limits of accuracy of the conductance measurements. For each solute, particular attention was paid to the rate of hydrolysis in solution. Measurements were made in order of increasing temperature and, periodically, the lowest temperature measurement was repeated. No significant change occurred during the period of the measurements, namely, 5 hours. In view of the labour involved in making large numbers of measurements at different temperatures, the measurements were restricted to four solutions of each solute, two from each sample, suitably spaced in concentration, at 5° intervals between 15° and 35°. A preliminary set of determinations with chloroacetic acid, and a general assessment of accuracy, indicated that this would be adequate.

Calculations of dissociation constants and of equivalent conductances at zero concentration were made by the method of Ives (*J.*, 1933, 731), based upon the Ostwald dilution law, the Onsager equation, and the Debye–Hückel limiting law.

The method is summarised in the equation

$$\Lambda + a\sqrt{C_i} = \Lambda_0 - \Lambda^2 C \,.\, 10^{-2A\sqrt{C_i}}/K(\Lambda_0 - a\sqrt{C_i}) \quad . \quad . \quad . \quad (2)$$

where a is the "Onsager slope," A the Debye–Hückel coefficient, and the other symbols have their usual significance. The method consists in finding by successive approximation the value of Λ_0 which, when incorporated in the quantity $x = \Lambda^2 C \,.\, 10^{-2A\sqrt{C_i}}/K(\Lambda_0 - a\sqrt{C_i})$ (with appropriate adjustments of the values of a and C_i), gives, on linear extrapolation to zero concentration, a limiting value of $y = \Lambda + a\sqrt{C_i}$ which is identical with the same value of Λ_0. Each successive extrapolation until this end is secured is carried out by the method of least squares. Values of the Onsager slopes and Debye–Hückel constants for the various temperatures used were calculated from Birge's fundamental constants (*Rev. Mod. Phys.*, 1941, **13**, 233), Wyman's dielectric constant data (*Phys. Rev.*, 1930, **35**, 623), and Bingham and Jackson's viscosity data (*Bull. Bur. Stand.*, 1918, **14**, 75), and these are shown in Table 2. Large-scale graphical plots of equation (2) showed no deviations

TABLE 2.

Temp.	Debye–Hückel constant, A	Onsager slope, a	Temp.	Debye–Hückel constant, A	Onsager slope, a
15°	0·50028	$0{\cdot}22485\ \Lambda_0 + 46{\cdot}942$	30°	0·51405	$0{\cdot}23104\ \Lambda_0 + 67{\cdot}466$
20	0·50456	$0{\cdot}22678\ \Lambda_0 + 53{\cdot}418$	35	0·51925	$0{\cdot}23338\ \Lambda_0 + 75{\cdot}019$
25	0·50908	$0{\cdot}22883\ \Lambda_0 + 60{\cdot}252$			

from strict linearity, and this is confirmed by the satisfactory constancy of the dissociation constants subsequently calculated for each concentration. The experimental equivalent conductances, Λ_0 values, and dissociation constants (in units mole l.$^{-1}$) are shown in

Table 3. Log Λ_0 was found to be a linear function of $1/T$, with deviations indicating a probable error in the Λ_0 values of about 0·2%.

TABLE 3.

	Equivalent conductance				Λ_0	$K \times 10^5$
Fluoroacetic acid						
$C \times 10^4$ (25°) =	15·8752	8·72730	4·06566	2·87610		
15°	240·10	268·61	296·76	305·92	335·88	278·93 ± 0·47
20	259·05	290·47	321·68	331·78	365·45	268·43 ± 0·41
25	277·43	311·49	345·74	357·00	394·20	259·59 ± 0·51
30	294·83	331·67	369·14	381·62	422·77	249·01 ± 0·43
35	311·10	350·80	391·56	405·29	450·70	237·86 ± 0·46
Chloroacetic acid						
$C \times 10^4$ (25°) =	27·8318	18·4848	11·4377	5·61169		
15°	171·04	193·83	220·40	257·10	334·30	142·98 ± 0·10
20	184·40	209·31	238·21	278·15	363·39	139·44 ± 0·11
25	197·32	224·04	255·32	298·65	392·01	135·94 ± 0·11
30	209·43	237·90	271·66	318·60	421·16	130·79 ± 0·01
35	220·73	251·03	287·15	337·48	449·34	125·94 ± 0·05
Bromoacetic acid						
$C \times 10^4$ (25°) =	28·0830	13·2823	10·2878	6·59113		
15°	165·24	206·45	220·47	243·72	331·44	133·31 ± 0·04
20	178·00	222·81	238·01	263·47	360·33	129·63 ± 0·04
25	190·06	238·33	254·87	282·47	389·03	125·30 ± 0·05
30	201·48	253·15	271·04	300·74	417·41	120·78 ± 0·07
35	212·08	267·18	286·17	318·15	445·42	115·88 ± 0·02
Iodoacetic acid						
$C \times 10^4$ (25°) =	20·8728	8·89308	6·02373	2·46310		
15°	148·02	194·62	216·36	261·81	332·45	71·90 ± 0·03
20	159·05	209·54	233·25	283·07	361·56	69·46 ± 0·02
25	169·41	223·74	249·32	303·62	390·41	66·80 ± 0·00
30	179·15	237·19	264·71	323·43	418·99	64·06 ± 0·01
35	188·19	249·78	279·24	342·37	447·10	61·26 ± 0·02

For the purpose of choosing the most representative values of the dissociation constants and of calculating the thermodynamic functions, the equation

$$\ln K = a + bT + cT^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

was fitted to the individual experimental results (*i.e.*, 20 values of ln K, from 4 solutions each at 5 temperatures) for each acid by the method of least squares. The choice of this equation was quite arbitrary and is justified solely by the fact that it fits the results within experimental error. It has been shown (Harned and Robinson, *Trans. Faraday Soc.*, 1940, **36**, 973) that several empirical formulæ fit such data equally well within the limits of accuracy in dissociation constant data yet attainable. Some of these formulæ imply that ΔC_p is independent of temperature (Everett and Wynne-Jones, *ibid.*, 1939, **35**, 1380; Briegleb and Bieber, *Z. Elektrochem.*, 1951, **55**, 250), but it is felt that this assumption can have no fundamental basis and that it might have to be discarded if sufficiently accurate measurements became available. It is hoped to explore this question in a later publication.

The results of these calculations are collected in Table 4, which shows the observed values of ln K, those calculated from the equations shown, the differences between these quantities, and the values of dissociation constants and Λ_0 finally selected. The fit of the equations was assessed in terms of the probable error in ln K, $\{\pm 0{\cdot}816\sqrt{[\Sigma q^2/(n-3)]}\}$, which had the values ±0·0024, ±0·0014, ±0·0005, and ±0·0004 for the acids in the order of Table 4. The higher error for the fluoroacetic acid results is no doubt associated with the greater difficulty in manipulating this intensely hygroscopic substance.

The thermodynamic functions of ionisation calculated from the interpolation equations are shown in Table 5. Since ΔH is derived from the temperature dependence of ln K, more uncertainty attaches to its value at the extremes of the temperature range; hence ΔH values are quoted only at 20—30°. A similar restriction applies to ΔC_p, which is thus

TABLE 4.

Temp.	ln $K_{obs.}$	ln $K_{calc.}$	Δ	$K \times 10^5$	Λ_0
Fluoroacetic acid					
		ln $K = -9{\cdot}4581 + 0{\cdot}0313701T - 0{\cdot}000065817T^2$			
15°	−5·8820	−5·8831	+0·0011	278·6	335·9
20	−5·9204	−5·9175	−0·0029	269·2	365·4
25	−5·9538	−5·9553	+0·0017	259·2	394·2
30	−5·9955	−5·9962	+0·0007	248·8	422·8
35	−6·0413	−6·0406	−0·0007	238·0	450·7
			Mean ±0·0014		
Chloroacetic acid					
		ln $K = -14{\cdot}4918 + 0{\cdot}0592736T - 0{\cdot}000110067T^2$			
15°	−6·5502	−6·5505	+0·0003	143·0	334·3
20	−6·5753	−6·5741	−0·0012	139·6	363·4
25	−6·6007	−6·6031	+0·0024	135·6	392·0
30	−6·6393	−6·6376	−0·0017	131·0	421·2
35	−6·6771	−6·6776	+0·0005	125·9	449·3
			Mean ±0·0012		
Bromoacetic acid					
		ln $K = -12{\cdot}0888 + 0{\cdot}0432874T - 0{\cdot}000084367T^2$			
15°	−6·6202	−6·6200	−0·0002	133·3	331·4
20	−6·6483	−6·6488	+0·0005	129·6	360·3
25	−6·6821	−6·6818	−0·0003	125·3	389·0
30	−6·7189	−6·7190	+0·0001	120·8	417·4
35	−6·7604	−6·7604	—	115·9	445·4
			Mean ±0·0002		
Iodoacetic acid					
		ln $K = -10{\cdot}8078 + 0{\cdot}0314747T - 0{\cdot}000066237T^2$			
15°	−7·2377	−7·2376	−0·0001	71·91	332·4
20	−7·2720	−7·2727	+0·0007	69·42	361·6
25	−7·3112	−7·3111	−0·0001	66·80	390·4
30	−7·3531	−7·3528	−0·0003	64·08	419·0
35	−7·3977	−7·3980	+0·0003	61·25	447·1
			Mean ±0·0003		

TABLE 5.

Temp.	$CH_2F{\cdot}CO_2H$	$CH_2Cl{\cdot}CO_2H$	$CH_2Br{\cdot}CO_2H$	$CH_2I{\cdot}CO_2H$
Gibbs free-energy change, ΔG (cal.)				
15°	3368	3750	3789	4143
20	3446	3828	3872	4235
25	3527	3911	3958	4330
30	3611	3997	4046	4428
35	3698	4088	4138	4529
Enthalpy change, ΔH (cal.)				
20°	−1232	− 897	−1054	−1256
25	−1390	−1123	−1239	−1416
30	−1558	−1362	−1435	−1585
Entropy change, ΔS (cal. deg.$^{-1}$)				
20°	−16·0	−16·1	−16·8	−18·7
25	−16·5	−16·9	−17·4	−19·3
30	−17·1	−17·7	−18·1	−19·8
Heat capacity change, ΔC_p (cal. deg.$^{-1}$)				
25°	−32·6	−46·4	−38·1	−32·9

quoted for 25° only. For this reason, no statement can be made concerning the temperature dependence of ΔC_p for these acids. An independent check on these results was made by plotting the observed value of ln K against $1/T$, drawing the best representative curves, and estimating their slopes graphically. The results so obtained showed mean deviations from those in Table 5 of ±0·5 cal. in ΔG, ±10 cal. in ΔH, ±0·05 cal. deg.$^{-1}$ in ΔS, and ±1 cal. deg.$^{-1}$ in ΔC_p; these deviations provide an assessment of the reliability of the data.

Comparison with existing data can only usefully be made for chloroacetic acid, for which previous dissociation constant data at 25° are listed in Table 6. It is believed that the new,

TABLE 6. *Data for chloroacetic acid.*

$K \times 10^3$	Method	Reference
151	Catalytic	Dawson, Hall, and Key, *J.*, 1928, 2844
141	Catalytic	Grove, *J. Amer. Chem. Soc.*, 1930, **52**, 1404
139·7	Conductance	MacInnes, Shedlovsky, and Longsworth, *Chem. Rev.*, 1933, **13**, 29
139·6	Conductance	Saxton and Langer, *J. Amer. Chem. Soc.*, 1933, **55**, 3638
137·8	E.M.F.	Wright, *ibid.*, 1934, **56**, 314
135·6	Conductance	Present investigation

somewhat lower, value is to be preferred. Greater attention has been paid to purity of materials in the present work and also, for the first time, the importance has been realised of using only freshly-prepared solutions and conducting the measurements with the least possible delay. The stock-solution method formerly used is highly disadvantageous when applied to these acids and especially to their sodium salts. Sodium chloroacetate hydrolyses faster than chloroacetic acid in aqueous solution (Senter, *J.*, 1907, **91**, 460) at a rate which increases with rising concentration (Kastle and Keiser, *Amer. Chem. J.*, 1893, **15**, 471), and this can be understood in terms of the complex hydrolytic reactions established for the analogous bromoacetic acid system (Dawson and Dyson, *J.*, 1933, **49**, 1133; Brooke and Dawson, *J.*, 1936, **497**). Although these observations relate to conditions other than those of very dilute aqueous solutions at 25°, it is quite clear that hydrolytic decomposition is a danger which attends ostensibly accurate physical measurements involving aqueous solutions of these substances. No satisfactory evidence is given in the earlier work that this hazard was successfully avoided. In the present investigation, a long series of trial measurements was made by the stock-solution method; the results were erratic and, in all cases, high compared with those finally obtained. No such trouble was encountered when each solution was made up rapidly and independently, immediately before measurement.

The value of the mobility of the chloroacetate ion derived from the present work (42·2) is appreciably higher than the value formerly assigned (39·8). This higher value is supported by the results from two independent extrapolations on other sets of chloroacetic acid measurements which each gave 42·0 for this mobility. Further, measurements made of the conductances of freshly-prepared solutions of sodium chloroacetate containing a trace of excess of acid gave, on extrapolation of Λ against $\sqrt{C}$, a value of 41·7. (The authors record their thanks to Mr. S. F. Feates for this result.) This agreement is reasonably satisfactory, for the remaining discrepancy is within the limit of accuracy of the Λ_0 determinations previously stated.

Wright's E.M.F. method (*J. Amer. Chem. Soc.*, 1934, **56**, 314) is open to strong objection for reasons which have already been indicated. Reference to the literature (Euler, *Ber.*, 1906, **39**, 2726; Senter, *J.*, 1910, **97**, 346; Cowdrey, Hughes, and Ingold, *loc. cit.*) and experiments conducted in these laboratories on the effects of silver ion and solid silver halide on the rate of hydrolysis of chloroacetic acid solutions lead to the view that little weight can be given to these results.

DISCUSSION

To facilitate discussion, results and related data for acetic acid and the four monohalogenoacetic acids in aqueous solution at 25° are collected in Table 7.

Comment is first required on the anionic mobility values, which at first sight would seem to be anomalous. Evidence of freedom from considerable error in the conductance measurements has already been presented. The extrapolation method of treating these results is but one way of finding the unique values of Λ_0 and K for a given electrolyte consistent with the Ostwald, Onsager, and limiting Debye–Hückel laws, and its validity is not open to question any more than the fundamental laws on which it is based. The properties originally claimed for the method (Ives, *loc. cit.*) have been confirmed (Kilpatrick, *J. Chem. Phys.*, 1940, **8**, 306) and it has been tested successfully by application to some of

the best available conductance data (Ives and Sames, *J.*, **1943**, 511). When applied to Shedlovsky's data (*J. Amer. Chem. Soc.*, **1932**, **54**, 1411) on acetic acid, it gives a value for Λ_0 of 391·0 (cf. Table 7), an agreement which is entirely satisfactory. Furthermore, the sensitivity of the method to error decreases with increasing strength of the electrolyte concerned (Belcher, *J. Amer. Chem. Soc.*, **1938**, **60**, 2744). It is therefore felt that the effects of halogen substitution on the mobility of the acetate ion which are revealed by the present work are real and significant, even though their interpretation may be a matter of some difficulty. It may also be pointed out that reference to Landolt–Börnstein's "Tabellen" reveals many such "unexpected" ionic mobility relationships.

TABLE 7.

	$CH_3{\cdot}CO_2H$	$CH_2F{\cdot}CO_2H$	$CH_2Cl{\cdot}CO_2H$	$CH_2Br{\cdot}CO_2H$	$CH_2I{\cdot}CO_2H$
$K \times 10^5$	1·754 (*a*)	259·2	135·6	125·3	66·80
pK	4·7560 (*a*)	2·5864	2·8689	2·9021	3·1752
Λ_0	390·6 (*b*)	394·2	392·0	389·0	390·4
l_0	40·8	44·4	42·2	39·2	40·6
ΔG (cal.)	6487 (*a*)	3527	3911	3958	4330
ΔH (cal.)	−112 (*a*)	−1390	−1123	−1239	−1416
ΔS (cal. deg.$^{-1}$)	−22·1 (*a*)	−16·5	−16·9	−17·4	−19·3
ΔC_p (cal. deg.$^{-1}$)	−33·9 (*a*)	−32·6	−46·4	−38·1	−32·9
μ, CH_2X	—	1·81 (*c*)	1·87 (*d*)	1·80 (*d*)	1·64 (*d*)
Field strength, E	—	0·197 (*e*)	0·190 (*e*)	0·177 (*e*)	0·153 (*e*)
Bond refractivity, C–X (c.c.)	1·69 (*f*)	1·72 (*f*)	6·53 (*f*)	9·37 (*f*)	14·55 (*f*)
$\Delta pK/E$	—	11·0	10·0	10·5	10·3

(*a*) Harned and Ehlers, *J. Amer. Chem. Soc.*, **1933**, **55**, 652. (*b*) Shedlovsky, *ibid.*, 1932, **54**, 1411 (*c*) Smyth and McAlpine, *J. Chem. Physics*, **1934**, **2**, 499. (*d*) Groves and Sugden, *J.*, 1937, 158. (*e*) Ives and Sames, *J.*, **1943**, 513. (*f*) Syrkin and Dyatkina, "The Structure of Molecules," Butterworths, London, **1950**, p. 201.

The K, pK, and ΔG values recorded show that the chloro- and bromo-acids resemble each other more closely than the other two members; this was already known from classical data and is paralleled by many other features of halogen chemistry. The other thermodynamic functions, however, show rather different relationships. Thus, $-\Delta H$ shows a minimum at the chloro-acid; $-\Delta S$, somewhat lower than for acetic acid, shows a smooth, almost asymptotic decrease from the iodo- to the fluoro-acid, whilst the $-\Delta C_p$ values show an entirely different trend, with a marked maximum at the chloro-acid. These relationships can at once be taken to indicate that the effect of polar substitution on acid strength is no simple function of purely energetic factors. Ives and Sames (*J.*, **1943**, 513), using the best data then available, attempted to show that the change in acid strength (ΔpK) caused by polar substitution is directly related to the strength of the field (E) set up in the appropriate direction by the polar bond of the substituent at the position supposedly occupied by the ionising hydrogen atom of the carboxyl group. The approximate constancy of the ratio $\Delta pK/E$ which was found was taken to support the view that the substitutional influence on acid strength operates, in these cases, by a direct field effect. The new data, shown in Table 7, do not strengthen the evidence for this, the values of $\Delta pK/E$ at 25° being made somewhat less constant.

A more fundamental approach to the problem may be suggested on the basis of the equation defining ΔG as a function of temperature, namely,

$$\Delta G = \Delta H_0 + \int_0^T \Delta C_p \,.\, dT - T\int_0^T \frac{\Delta C_p}{T} \,.\, dT - T\Delta S_0 \quad . \quad . \quad . \quad . \quad (4)$$

in which the term ΔH_0 should properly include the electrostatic energy terms affecting the free energy of ionisation. Since, however, this term is not accessible, the next best procedure would seem to be to discuss such energy effects in terms of ΔH. If this is done for the four halogenoacetic acids on lines comparable with those just followed, the ratios of the terms ($\Delta H_{\text{unsubs.}} - \Delta H_{\text{subs.}}$) to the field strength at the site of ionisation must be examined. These are, absolute magnitudes being disregarded, 6·4, 5·3, 6·4, and 8·6 in the order fluoro- to iodo-acetic acid. This leaves no doubt that, whilst a direct field effect may,

in these cases, be a major one, it is far from adequate to explain all the facts. No quantitative treatment of this problem on simple lines appears to be possible, but discussion of relative $-\Delta H$ values for the dissociation of weak acids may be profitable. The ionisation of all four halogenoacetic acids is more exothermic than that of acetic acid, in line with their greater ease of ionisation. The order of the $-\Delta H$ values, however, except for fluoroacetic acid, is the reverse of that to be expected from the field due to the substituent at the seat of ionisation. This suggests that the minimum in $-\Delta H$ which occurs at the chloro-acid is due to the joint effect of two factors, both tending to enhance acidity, one of which increases from iodo- to fluoro-acetic acid and the other in the opposite direction. The first of these must be the direct field effect, and the other is suggested by inspection of the bond refractivities shown in Table 7. For fluorine, the polarisability of the substituent is hardly greater than that of hydrogen, but it increases rapidly with the atomic number of the halogen. During ionisation, the carboxyl group in its normal or transition state will set up a field embracing the whole of the molecule, and any polarisable atom situated within the critical cone of semi-angle 55° with respect to the axis of the primary (carboxyl) dipole will develop an induced moment in such a direction as to enhance the field promoting ionisation. Similarly, for the anion, a polarisable residue will have an electrostatic effect tending to hinder the return of the proton. An analogy is to be found in the effect of a substituent olefinic or aromatic group on the strength of acetic acid (Ives, Linstead, and Riley, *J.*, 1933, **561**; Baker, Dippy, and Page, *J.*, 1937, 1774), where the polarisability effect, if not the only one, is undoubted.

Attention may now be turned to the entropy and heat-capacity changes accompanying the ionisation of these acids. A tentative interpretation of the observed trend of these values may be based upon the assumption of the solvation of the undissociated acid molecules by virtue of the polar carbon–halogen bonds which they contain. Such dipole solvation, approaching zero for the carbon–iodine bond, is likely to increase from iodo- to fluoro-acetic acid at a rate faster than would appear from the bond moments. Such solvation will be controlled by the intensity of the field at the halogen atom, and this will be an inverse function of atomic size. In the corresponding ions, however, not only may the larger halogen atoms exercise a screening effect, sterically hindering the approach of solvent molecules to the site of the negative charge, but the presence of this charge may so modify the dipole solvation as to cause a general levelling of the effect. In other words, it seems reasonable to suppose that the molecules show a greater individuality in regard to solvation than the ions. The ***increase*** in the degree of solvation which accompanies ionisation may, by these arguments, be expected to be rather less for the substituted acids than for the unsubstituted acid and, in general, to run parallel with the observed values of $-\Delta S$.

TABLE 8.

Acid	M. p.	Equiv., obs.	Equiv., calc.	Acid	M. p.	Equiv., obs.	Equiv., calc.
$CH_2F{\cdot}CO_2H$	35·4—35·5°	78·03 ± 0·04	78·04	$CH_2Br{\cdot}CO_2H$	47·8—48·2°	138·95 ± 0·07	138·96
$CH_2Cl{\cdot}CO_2H$ (α-form)	62·3—62·7	94·46 ± 0·05	94·50	$CH_2I{\cdot}CO_2H$	81·6—81·9	186·00 ± 0·09	185·95

It seems evident that the endothermic desolvation process, and the new degrees of freedom of the solvent molecules which are liberated in this process, must make an important contribution to heat capacity (cf. Eigen and Wicke, *Z. Elektrochem.*, 1951, **55**, 354). Heat capacity may then be a function, *inter alia*, both of the extent and of the stability of solvation. For the anions of these acids, it has been found that the quantity $(\mathrm{d} \ln l_0/\mathrm{d}T - \mathrm{d} \ln \phi/\mathrm{d}T)$, where ϕ is the fluidity of water, has values at 25° of 68, 196, 237, and 243 × 10^{-5} deg.$^{-1}$ for the fluoro-, chloro-, bromo- and iodo-acetate ions respectively. These figures, representing the increase of ionic mobility over and above that due to the increase of fluidity, possibly give some indication of the relative vulnerability of these ions to desolvation with rise of temperature. If, then, desolvation should contribute significantly to the heat capacity of the ionised system, ΔC_p for ionisation should decrease in its negative value in this order. This appears to be the case, except that the fluoro-compound, as is so often the case, is exceptional. But molecular dipole solvation has

already been suggested as a factor significantly affecting the entropy of ionisation, and this is as likely to affect ΔC_p. If the heat capacity of the un-ionised system is influenced mainly by the extent of this, probably rather unstable, kind of solvation, this would again be consistent with the same trend of ΔC_p values. In this case, however, the exceptional behaviour of fluoroacetic acid finds a possible explanation in a special stability of the dipole solvation centred on the fluorine atom, for hydrogen bonding might well be involved. The fact that the lower alkyl fluorides "are somewhat unexpectedly soluble in water" (Dyson, "Manual of Organic Chemistry," Longmans, 1950, p. 231) may be relevant in this connection.

Although much of the above discussion is tentative and exploratory, it emphasises the probability that all the terms contained in equation (4) have their own physical significance as factors which determine acid strength.

Experimental

The Bridge.—An oscillator of the type used by Shedlovsky (*J. Amer. Chem. Soc.*, 1930, **52**, 1793), giving an output at eight frequencies from 1150 to 5250 c./sec., of very low harmonic content, was loosely inductively coupled to a feeder circuit consisting of two 1000-ohm potentiometers spanning the oscillator input. Between the moving contacts of these potentiometers there was available a signal of any desired phase and amplitude on either side of earth potential. This simple device has considerable advantages. The r.m.s. potential difference supplied to the bridge was measured by means of an instrument rectifier and a suitable micro-ammeter incorporated in the feeder unit; the latter supplied a Wagner earthing circuit of conventional design. The bridge ratio arms consisted of two 1000-ohm Cambridge Constantan non-inductive resistors connected together by means of a shunted potentiometer designed to adjust the ratio to equality within one part in 10^6. A Cambridge Constantan decade resistance box, adjustable to 0·0001 ohm, was used, and this was internally calibrated periodically during the course of this work and compared, by a D.C. method, with a standard box kindly lent by Dr. H. R. Nettleton. The Cambridge box was found to have zero temperature coefficient; its frequency dependence was also zero, except for the 1000-ohm decade, so that separate calibration at different frequencies was necessary only in this case. Frequent routine cleaning of the box contacts was found to be essential. Provision was made for shunting either bridge arm with mica or air condensers. The output from the bridge was fed to an amplifier (Ives and Pittman, *Trans. Faraday Soc.*, 1948, **44**, 644) of sensitivity adequate to allow bridge settings to one part in 10^6. The bridge was used alternatively for platinum thermometry, and all resistance measurements were made by the "four-leads" method (Smith, *Phil. Mag.*, 1912, **24**, 541; Mueller, *Bull. Bur. Stand.*, 1916/17, **13**, 547). The switch-gear for selecting either component of the double cell or the thermometer, for providing the shunts necessary for measuring very high resistances (*e.g.*, of cells containing conductance water), or for the reversals of connections involved in the "four-leads" method fell into two categories. The switches of which the contact resistances were cancelled by the "four-leads" method were of the ordinary multipole radio type; the others were mercury switches using conductors of very heavy cross-section. A residual correction of +0·0019 ohm for uncancelled leads resistance was applied where significant. The advantages of this system have already been mentioned and its success was checked by measurements of series–parallel resistance networks set up from individually-measured components; observed and calculated resistances invariably agreed to the highest order of accuracy. This device also provided a check on the accuracy of the box calibration.

Temperature Measurement.—No description could be found of a resistance thermometer of adequate sensitivity, and none was available commercially. A brief description of a thermometer made for the purpose, in accordance with the criteria given by Mueller ("Temperature, its Measurement and Control in Science and Industry," Reinhold, New York, 1941, p. 162) and by the National Physical Laboratory ("The International Temperature Scale of 1948," N.P.L., 1950, p. 6), may therefore be of interest. A non-inductive winding of 4 m. of 42 S.W.G. "thermopure" platinum wire was held by an octagonal mica former, each of the 64 turns resting in 1-mm. deep slots in the eight blades of the former. Close to the winding, each end of the wire was bifurcated by welding, and the four leads so produced were welded to 20-cm. lengths of gold wire, which were in turn welded to heavy silver output leads. The gold wires were threaded through 13 mica discs, fitting into a Pyrex tube which, flanged at its ends, confined the thermometer element in its Pyrex sheath. The annular space between this inner tube and the sheath was fitted with spaced mica rings. The upper end of the sheath was sealed

to a B.24 cone, by which the thermometer could be fitted into an all-glass hypsometer, and was closed by a polystyrene plug which was sealed in with picein wax. The lower end of the sheath was attached to a high-vacuum system, and the thermometer was pumped out with the winding at bright red heat. Slow cooling was effected during several days, after which dry air was admitted, and the sheath sealed.

The thermometer was calibrated at the ice- and steam-points and at the transition point of sodium sulphate. The limit of accuracy was set by an irreducible uncertainty of $\pm 0{\cdot}002°$ in the steam-point, arising from the limitations of barometric readings. Local barometric readings were corrected by pressures ascertained from the Meteorological Office, Kingsway, and from Kew Observatory. The constants of the thermometer were: $R_{100} - R_0$, 12·8502 ohms; R_{100}/R_0, 1·3913; δ, 1·498; these are better than the criteria laid down by the N.P.L. (*loc. cit.*) for precise platinum thermometry. The final equation relating temperature to the resistance of this thermometer was

$$t = \frac{100(R_t - 32{\cdot}8423)}{12{\cdot}8502} + 1{\cdot}498\left(\frac{t}{100} - 1\right)\frac{t}{100} \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Temperatures derived from this equation were checked against two points on a bomb-calorimeter thermometer certified by the N.P.L. to $\pm 0{\cdot}002°$; agreement was within $\pm 0{\cdot}001°$. Further checks at intervals against thermometers standardised at the N.P.L. to $\pm 0{\cdot}005°$ between 15° and 35° showed an agreement which averaged $\pm 0{\cdot}002°$ and in no case exceeded $\pm 0{\cdot}004°$.

Temperature Control.—A 45-l. Perspex tank, thermally insulated with slag wool, was filled with Silvertown Lubricants transformer oil B.30, which was kept anhydrous by silica gel and circulated vigorously by two stirrers. A spiral toluene–mercury regulator operated a 300-w. Robertson lamp as heater through an electronic relay (Taylor, *J.*, 1951, 232). Cooling was provided by circulation of refrigerated glycol at a controlled rate through a copper cooling coil. Temperature fluctuation was negligible.

The Conductance Cell.—The double cell is illustrated in the Figure. The difficulty of maintaining a rigid electrode assembly whilst avoiding the leakages inseparable from massive platinum–Pyrex seals was met by using spherical-section platinum cups 2·5 cm. in diameter, 1 cm. deep, and 0·005 cm. thick as electrodes. These were drilled in the centre to allow free flow of solution, and near the edges to allow the insertion of Pyrex anchoring studs, subsequently fused to the inside of a Pyrex envelope. Electrical connection was made by welding on to each electrode two fine tags of platinum foil 0·001 cm. thick, at the edges of the central drilling. These were pinch-sealed into thin-walled Pyrex contact tubes, a procedure known to provide vacuum-tight seals (Campbell, *J. Amer. Chem. Soc.*, 1929, **51**, 2419; Hills and Ives, *J.*, 1951, 305). These tags were in turn welded to 28 S.W.G. platinum wires, which, at the upper ends of the contact tubes, were soldered to copper leads passing out through brass cones which were sealed into the contact tubes with sealing-wax. It may be noted that the resistance of the cell leads was about 2·5 ohms, but that this was cancelled out completely by the use of the " four-leads " method. The double cell, after grey-platinisation of the electrodes *in situ*, cleaning and steaming, was mounted permanently in the thermostat bath, and was not again subjected to any drastic cleaning procedure.

Conductance Water.—Water was prepared in a still of the Stuart and Wormwell type (*J.*, 1930, 85), in which steam from distilled water containing potassium hydroxide and permanganate was passed successively through a long packed column, a phosphoric acid scrubber, and steam traps into a vertical Vitreosil condenser, where it was mixed with a rapid stream of oxygen-free nitrogen which had passed through an efficient purification train. Water was not collected until a conductance cell attached to the still indicated a specific conductance less than $0{\cdot}08 \times 10^{-6}$ ohm^{-1}.

Potassium Chloride.—The very pure potassium chloride prepared by Hills and Ives (*J.*, 1951, 305) was used for the cell-constant determination. Comparison with pure silver by analysis had given an atomic ratio Cl/Ag = 0·99992.

Halogenoacetic Acids.—Fluoroacetic acid was supplied by Dr. B. C. Saunders of Cambridge University, to whom the authors express their thanks. This acid is intensely hygroscopic and liquefies completely on short exposure to air. The sample was dehydrated in a high-vacuum system, sublimed, and recrystallised five times from very pure anhydrous benzene in a totally enclosed, all-glass apparatus (Sample A). A second sample (B) was obtained by fractional sublimation *in vacuo* between temperatures of 30° and 0°. The other halogeno-acids were obtained from commercial sources and were purified by similar methods to yield samples A and B. M. p.s were determined in m. p. tubes attached to a high-vacuum apparatus and immersed

in a large stirred water bath, the temperature of which was raised at a constant rate of 0·1° per min. Totally immersed N.P.L.-calibrated thermometers were used. It may be noted that, because of polymorphism and incipient decomposition in the melt, sharpness of m. p. cannot be taken as a criterion of purity, except for the fluoro-acid. Equivalents were determined by titration, very pure "Calorimetric Standard" benzoic acid, repeatedly crystallised from conductance water and dried over phosphoric oxide, being used as the primary standard. The results of these determinations are shown in Table 8; these m. p.s should be regarded as new data.

Procedure.—Solutions were prepared in 1-l., two-necked Pyrex flasks. These were steamed, washed with conductance water, oven-dried, cooled, filled with pure, dry nitrogen, and weighed. Solutes were weighed by difference directly into these flasks, by using an Oertling 141 semi-micro-balance and weights calibrated to 0·01 mg. against N.P.L. standards. Conductance water was introduced directly into the solution flask from the still against a counter-current of purified nitrogen. The flask was re-weighed, by use of an Oertling balance of maximum load 2 kg. and sensitivity ±1 mg., and the solution was thoroughly mixed, wetting of ground joints being carefully avoided. Appropriate buoyancy corrections were applied to all weighings, and concentrations in moles per litre were calculated at each temperature.

The conductance cell was kept permanently filled with conductance water, which was expelled by pressure of nitrogen before use. All-glass connections to the cell, except for short poly(vinyl chloride) connections with screw-clips, used as greaseless taps, enabled the cell to be filled with, and emptied of, solution by manipulating pressures of highly purified nitrogen. The cell was filled with solution and emptied again five times before the final filling on which, after temperature equilibration, readings of conductance were made. Measurements were made successively at 15°, 20°, 25°, 30°, and 35° with, when appropriate, a final return to 15° as a check. It was found advantageous to take each measurement at some arbitrary temperature within about 0·02° of the precise temperature desired, and then to apply an adjustment by means of a determined temperature coefficient of conductance.

The conductance of the water used in preparing the solutions was found by taking measurements on the section of the cell of lower constant, shunted by a standard resistance. Solvent correction was additive for potassium chloride solutions and zero for the acid solutions.

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BIRKBECK COLLEGE, W.C.1. [*Received, February 2nd,* 1955.]

The Chemistry of the Aristolochia *Species. Part II.* Some Rearrangements of Aristolactone.*

By J. B. STENLAKE and W. D. WILLIAMS.

[Reprint Order No. 6002.]

Aristolactone, $C_{15}H_{20}O_2$, is an αβ-unsaturated γ-lactone containing two other isolated double bonds. Hydrogenation gave first dihydroaristolactone and, finally, the hexahydro-compound. Base-catalysed rearrangement of aristolactone in ethanol and methanol yielded γ-keto-esters. Acid-catalysed isomerisation of aristolactone gave *iso*aristolactone which was converted on hydrogenation first into dihydro- and then into hexahydro-aristolactone.

IN Part I * we described the isolation from the roots of *Aristolochia reticulata* of a crystalline lactone, aristolactone, $C_{15}H_{20}O_2$.

Aristolactone, exhibited a light-absorption maximum at 211 mμ (ε, 11,500) attributed to an αβ-unsaturated ester or lactone function; failure to isolate an alcohol, and the quantitative recovery of the acidic fraction after hydrolysis supported the assignment of a lactone. A small portion only of the acid crystallised, and this gave a crystalline, but unstable, *S*-benzylthiuronium salt. The bulk of the acid was unstable, rapidly changing into a neutral oil, which could not be characterised. Determination of the iodine value indicated the

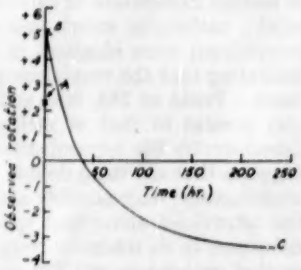
* Part I, *J. Pharm. Pharmacol.*, 1954, **6**, 1005.

equivalent of 2·3 ethylenic bonds in aristolactone, the fractional value being attributed to slow addition of halogen at the double bond associated with the lactone carbonyl group.

The presence of a third double bond was confirmed by microhydrogenation. Hydrogenation on a larger scale was slow and yielded the saturated (tetranitromethane) hexahydroaristolactone, m. p. 103·5—104°. Subsequent hydrogenations, however, yielded mixtures of two different crystalline forms, needles, m. p. 99—100°, and plates, m. p. 100—102°. The chemical identity of these two materials was confirmed by microanalysis, by their infrared spectra, and by hydrolysis to the same hydroxy-acid (see below). The mixed m. p. curve showed a maximum in the range 101—104°. The large negative shift of optical rotation which accompanies the hydrogenation of aristolactone is attributed to the presence of one or more asymmetric centres in close association with a double bond (cf. Chanley and Polgar, *J.*, 1954, 1003).

Hexahydroaristolactone, unlike aristolactone (see below), was stable to cold, but was readily hydrolysed by hot ethanolic potassium hydroxide. The hydroxy-acid, obtained from both crystalline forms of hexahydroaristolactone, was readily reconverted into the parent lactone (needle form) when heated just above its melting point in a sealed tube. Trace amounts of a second, saturated, acid, m. p. 121—122°, were also isolated from the hydrolysis products of hexahydroaristolactone. This acid, however, could not be lactonised, but underwent slow decomposition.

FIG. 1.



In carbon tetrachloride, aristolactone showed a strong band at 1770 cm.$^{-1}$ (1736 cm.$^{-1}$ in paraffin mull), characteristic of an $\alpha\beta$-unsaturated γ-lactone, with the expected shift to 1780 cm.$^{-1}$ (1750 cm.$^{-1}$ in paraffin mull) in hexahydroaristolactone. Marked changes following hydrogenation are also reflected in the ester-group absorptions in the region 1000—1250 cm.$^{-1}$, the two bands at 1034 and 1064 cm.$^{-1}$ of aristolactone being replaced by a single band at 1167 cm.$^{-1}$ in hexahydroaristolactone. A strong band at 890 and a medium one at 1650 cm.$^{-1}$, which are present in the spectrum of aristolactone (in carbon disulphide) and absent from that of hexahydroaristolactone are attributed to a vinylidene group. This conclusion has been confirmed by the identification of formaldehyde as a product of ozonolysis. Medium bands at 782 and 840, and a weak band at 800 cm.$^{-1}$ present in the spectrum of aristolactone, are likewise absent from that of hexahydroaristolactone, and suggest that of the two remaining double bonds, one at least is tetrasubstituted.

Hydrolysis of aristolactone was accompanied by marked changes of optical rotation, indicative of structural alterations more complex than the opening of the lactone ring. Treatment with cold ethanolic potassium hydroxide caused an initial positive shift up to the maximum which was relatively rapid, being complete within *ca.* 40 min. The succeeding fall was very much slower, a constant negative value being reached only after about 10 days. Titration of a series of aliquot portions, withdrawn during the reaction, showed that, whereas the initial increase of rotation did not involve utilisation of alkali, the succeeding fall in rotation was accompanied by neutralisation of one equivalent. The first reaction is therefore regarded as a base-catalysed rearrangement, and the second reaction as the hydrolysis of the primary product.

The product, isolated in high yield at the point of maximum rotation, was a neutral substance, apparently formed by the addition of the elements of ethanol to aristolactone. Repeated recrystallisation of the product from acetone–water showed that ethanol was not present as solvent of crystallisation. The infrared spectrum (paraffin mull) showed peaks at 1726 and 1186 cm.$^{-1}$ (ester carbonyl); peaks at higher frequencies which could be associated with the original lactone function were absent. The presence of an isolated carbonyl group was established by a low-intensity absorption maximum at 291 mμ (ε, 250), and confirmed by a shoulder at 1704 cm.$^{-1}$.

The formation and properties of this product are characteristic of keto-esters formed by

alkaline rearrangement of other αβ-unsaturated lactones (Paist, Blout, Uhle, and Elderfield, *J. Org. Chem.*, 1941, **6**, 273; McKean and Spring, *J.*, 1954, 1989), and establish the partial structures (I and II; R = Et) for aristolactone and this ester, respectively. The loss of a double bond in the formation of the ester, ethyl oxoaristate, was confirmed by micro-hydrogenation and by determination of iodine value. Hydrogenation gave an oily saturated ester (equivalent, 281), which on hydrolysis yielded an acid also as an oil. This oil showed an absorption maximum at 287 mμ (ε 51), consistent with the carbonyl group's being resistant to hydrogenation under the conditions used.

(I) (II)

Treatment of aristolactone with methanolic potassium hydroxide similarly gave methyl oxoaristate. Since this ester could be isolated pure more readily than the ethyl ester it was used in preference to the latter in all our later experiments. The absorption spectrum of methyl oxoaristate in carbon disulphide showed peaks at 1735 and 1150—1200 (broad band; carboxylic ester) and at 1720 cm.$^{-1}$ (ketone). Peaks at 890 and 1650 cm.$^{-1}$ (vinylidene) were identical in position and intensity with those of the parent lactone, indicating that the vinylidene group was apparently unaffected by the alkaline rearrangement. Peaks at 782, 800, and 840 cm.$^{-1}$ observed in the spectrum of aristolactone were also present in that of methyl oxoaristate, though much reduced in intensity. This demonstrates the tetrasubstitution of the second double bond of methyl oxoaristate and suggests that the third double bond, which is eliminated in the alkaline rearrangement of aristolactone, may possibly also be tetrasubstituted. These conclusions are supported by the ultraviolet absorption spectra, which showed a small shift in the maximum and a reduction in its intensity from 211 mμ (ε, 11,500) in aristolactone to 209 mμ (ε, 6360) in methyl oxoaristate and 209 mμ (ε, 7000) in ethyl oxoaristate. The position and intensity of the maxima for methyl and ethyl oxoaristate are characteristic of a tetrasubstituted ethylenic bond (Halsall, *Chem. and Ind.*, 1951, 867).

Further evidence for the rearrangement postulated comes from the observation that the bands in the spectrum of hexahydroaristolactone at 953 and 1010 cm.$^{-1}$, attributed to a *cyclo*hexane ring (Marrison, *J.*, 1951, 1614), were replaced in the spectrum of methyl oxoaristate by one at 1100 cm.$^{-1}$ (*cyclo*hexanone derivatives; cf. Lécompte, *Compt. rend.*, 1945, **221**, 50). These bands also provide evidence for the presence of a second ring in aristolactone, and support the thesis (based upon its formulation as $C_{15}H_{20}O_2$ with three double bonds) that the parent lactone is bicyclic, so that the second ring can be tentatively assigned as six-membered.

Ethyl oxoaristate was first obtained by the catalysed reaction of ethanolic ammonia on the lactone. Ammonia is known to form adducts with certain αβ-unsaturated lactones (Hansen, *Ber.*, 1931, **64**, 67; Ruzicka and Pieth, *Helv. Chim. Acta*, 1931, **14**, 1090), and although aristolactone failed to form such an adduct, a catalysed reaction with ethanolic ammonia in the presence of traces of zinc dust gave ethyl oxoaristate. The reaction, which was followed polarimetrically, was complete in *ca.* 72 hours, the rotation having then reached a maximum. If permitted, this reaction also continued with the same slow fall of rotation observed when ethanolic potassium hydroxide had been used. Methanolic ammonia, in the presence of zinc dust, reacted much more rapidly to give methyl oxoaristate.

Aristolactone was isomerised by boiling glacial acetic acid to a new lactone, *iso*aristolactone. Much resinification occurred and some material was recovered as an oil of similar rotation to that of *iso*aristolactone, but which was unchanged by further treatment with glacial acetic acid. The ultraviolet absorption spectrum of *iso*aristolactone was similar to that of aristolactone but also showed a low-intensity maximum at 272 mμ (ε, 640).

*iso*Aristolactone was non-aromatic (yellow colour with tetranitromethane), and was hydrolysed only very slowly by boiling ethanolic potassium hydroxide. The seat of the isomerisation is therefore in or near the lactone ring, and *iso*aristolactone cannot be represented as an αβ-unsaturated lactone, with an endocyclic double bond as in (I). Complete hydrogenation of *iso*aristolactone confirmed the presence of three ethylenic bonds and gave hexahydroaristolactone as sole product, indicating that the isomerisation was not a stereoisomeric change. The hydrogenation showed a definite break in rate of hydrogen uptake after the rapid absorption of 1 mol., and then gave a dihydro-compound in excellent yield. This difference from aristolactone, which showed a break in uptake after the slow absorption of 2 mols., supported the hypothesis that a double-bond shift had occurred in the isomerisation. This was confirmed by the isolation of dihydroaristolactone (identical with the dihydro-compound from *iso*aristolactone) from the controlled hydrogenation of aristolactone.

Spectroscopic evidence supports the view that the same double bond is involved in both acid and alkaline rearrangements. In carbon disulphide *iso*aristolactone showed typical vinylidene bands at 892 (s) and 1655 cm.$^{-1}$ (m) of the same intensity as those in the parent lactone. Bands at 787 (m) and 842 cm.$^{-1}$ (m) (tetrasubstituted ethylene), however, were of similar intensity to those recorded for methyl oxoaristate (reduced intensity compared

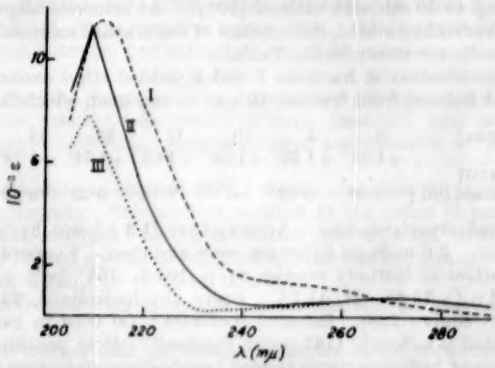


FIG. 2.
I, Aristolactone.
II, *iso*Aristolactone.
III, Dihydroaristolactone.

with aristolactone). Dihydroaristolactone showed similar bands, and, moreover, exhibited a maximum at 209 mμ (ε, 7800) (isolated tetrasubstituted ethylene). Further evidence for the double-bond shift is adduced from comparison of the ultraviolet absorption spectra of aristolactone and *iso*aristolactone (Fig. 2). The broader maximum shown by aristolactone at 211 mμ is in accord with that expected for the summation of the band due to the isolated tetrasubstituted ethylene at 209 mμ with that at a longer wavelength due to the αβ-unsaturated lactone function (cf. Barton and de Mayo, *J.*, 1954, 887). The much more sharply defined maximum at 209 mμ in *iso*aristolactone in which the carbonyl group is not αβ-unsaturated, is regarded as the summation of two similar peaks, both at the same wavelength, one being due to the isolated tetrasubstituted double bond as in dihydroaristolactone. Comparison of the molecular extinction coefficients of dihydroaristolactone and *iso*aristolactone suggests that the new double bond in *iso*aristolactone may be trisubstituted.

EXPERIMENTAL

M. p.s are uncorrected. Rotations were determined in absolute ethanol (unless otherwise stated) in a 1-dm. tube. Ultraviolet absorption spectra were determined in absolute ethanol on a Hilger Uvispek photoelectric spectrophotometer; infrared absorption spectra by using a recording double-beam infrared spectrometer, built in this College by Dr. I. A. Brownlee (*J. Sci. Instr.*, 1950, **27**, 215). We are indebted to Mr. A. Pajaczkowski and Dr. G. Houghton for these measurements and to Mr. W. McCorkindale and Dr. A. C. Syme for the microanalyses.

Aristolactone.—This was isolated from the petrol-soluble extract of *Aristolochia reticulata* as described in Part I and formed needles (from acetone–water), m. p. 110·5—111°, $[\alpha]_D^{14}$ +156·4° (*c*, 1), $\lambda_{max.}$ 211 mμ (ε, 11,500) [Found : C, 77·5; H, 8·8%; equiv. (by hydrolysis), 233; *M* (Rast), 227 ± 13. Calc. for $C_{15}H_{20}O_2$: C, 77·6; H, 8·7%; equiv., 232; *M*, 232). Infrared spectrum : (*a*) 0·5M in carbon tetrachloride—peaks at 1770 (αβ-unsaturated γ-lactone), 1034, and 1060 (ester function); (*b*) in paraffin mull—peak at 1736 (αβ-unsaturated γ-lactone); (*c*) 0·5M in carbon disulphide—peaks at 1650 (m) and 890 (s) (vinylidene), 840 (m), 800 (w), and 782 (m) cm.$^{-1}$ (tetrasubstituted ethylene). The iodine value (determined by the method of the British Pharmacopœia) was equivalent to 2·3 double bonds.

Hydrolysis. (*a*) Aristolactone (216 mg.) was refluxed for 30 min. with ethanolic potassium hydroxide (0·66N ; 3 ml.), and the solution, after acidification, extracted with ether to yield a viscous oil (207 mg.). This partly crystallised to an acid, m. p. 118°. The residual oil (140 mg. ; equiv., 363), after neutralisation with 0·1N-sodium hydroxide and extraction with light petroleum, yielded a neutral oil (52 mg.); acidification of the aqueous solution and extraction with ether gave an acidic oil (87 mg.) similar to that described above.

(*b*) Aristolactone (72·8 mg.) was dissolved in cold ethanolic potassium hydroxide (0·66N ; 5 ml.) and the solution examined polarimetrically (1 dm. tube; 13°). The rotations observed are plotted in Fig. 1.

(*c*) Aristolactone (261 mg.) was dissolved in ethanol (90%) which had been freed from carbon dioxide, freshly prepared N-ethanolic potassium hydroxide (3 ml.) was added, and the solution made up to 50 ml. with ethanol (90%). At intervals aliquot parts (5 ml.) were titrated with 0·05N-hydrochloric acid, the rotation of the alkaline solution being determined at the same time. The results are shown in the Table.

Neutralisation of fractions 7 and 8 yielded ethyl oxoaristate, m. p. 55° (see below). The product isolated from fraction 10 was an oily acid, which failed to crystallise.

Time (min.) ...	0	5	10	15	25	35	55	75	30 (days)	38 (days)
$[\alpha]_5^{18}$	+1·05°	+1·38°	+1·53°	+1·65°	+1·74°	+1·78°	+1·81°	+1·79°	−0·30°	−0·48°
0·05N-KOH neutralised (ml.)	0·00	0·02	—	0·13	0·23	0·22	0·31	0·31	2·22	2·34

Hexahydroaristolactone.—Aristolactone (1·3 g.) was hydrogenated in ethanol in presence of platinum; 3·0 mols. of hydrogen were absorbed. Evaporation of the solvent gave *hexahydroaristolactone* in feathery needles, m. p. 103·5—104°, $[\alpha]_D^{17}$ +3° (*c*, 1·2%), from light petroleum [Found : C, 75·65; H, 11·1%; equiv. (by hydrolysis), 233. $C_{15}H_{26}O_2$ requires C, 75·6; H, 11·0%; equiv., 238]. Infrared spectrum : (*a*) 0·5M in carbon tetrachloride—peaks at 1780 (saturated γ-lactone), 1167 (ester function); (*b*) in paraffin mull—1750 (saturated γ-lactone). Subsequent hydrogenations yielded hexahydroaristolactone first in needles, m. p. 99—100°, and then in plates, m. p. 100—102°, $[\alpha]_D^{17}$ +3° (Found : C, 75·2; H, 11·4%). The infrared spectra were identical with that described above. A mixture of the needles and the plates had m. p. 101—104°.

Dihydroaristolactone.—Aristolactone (276 mg.) was hydrogenated in ethanol in presence of palladium–charcoal, the reaction being stopped after the absorption of 1 mol. of hydrogen. Evaporation of the solvent gave dihydroaristolactone, m. p. 79—80·5°, $[\alpha]_D^{17}$ −77° (from light petroleum).

Hydrolysis of Hexahydroaristolactone.—(*a*) Hexahydroaristolactone (needles; m. p. 103·5—104°; 121 mg.) was refluxed with ethanolic potassium hydroxide (0·66N ; 5 ml.) for 30 min., and the solution acidified and extracted with light petroleum to yield plates, m. p. 86—87° (from light petroleum), $[\alpha]_D^{16}$ +16° (*c*, 1·6) (Found : C, 70·3; H, 11·2. $C_{15}H_{28}O_3$ requires C, 70·3; H, 11·0%). Fractional crystallisation of the mother liquors yielded a small quantity of a second acid, in short needles, m. p. 121—122°, insufficient for characterisation. The acid did not give a yellow colour with tetranitromethane.

(*b*) Hexahydroaristolactone (plates; m. p. 100—102°; 300 mg.) was refluxed with ethanolic potassium hydroxide (0·66N ; 5 ml.) for 30 min. The *product* (Found : equiv., 239. $C_{15}H_{28}O_3$ requires equiv. 238) isolated as in (*a*), formed plates, m. p. 86—87° undepressed on admixture with the acid obtained from (*a*).

The acid (m. p. 86—87°; 32 mg.) was heated in a sealed tube at 100° for 3 hr. over phosphoric oxide. After sublimation, hexahydroaristolactone was isolated as feathery needles, m. p. and mixed m. p. 100—103°.

Ethyl Oxoaristate.—Aristolactone (156·5 mg.) was dissolved in a mixture of N-ethanolic potassium hydroxide (2 ml.) and ethanol (90%; 25 ml.); the solution was neutralised with

0·1N-hydrochloric acid as soon as the optical rotation reached a maximum. Dilution with water yielded *ethyl oxoaristate* (126 mg.) in needles, m. p. 56—57° (from acetone–water), $[\alpha]_D^{19}$ +317° (*c*, 1), $\lambda_{max.}$ 209 mμ (ε, 7000) and 291 mμ (ε, 250) (Found: C, 73·1; H, 9·4. $C_{17}H_{26}O_3$ requires C, 73·3; H, 9·3%). Infrared spectrum in paraffin mull: peaks at 1726 and 1186 (ester carbonyl); 1704 (sh) cm.$^{-1}$ (ketone). Iodine value equivalent to 2·5 double bonds.

Hydrogenation of Ethyl Oxoaristate.—(*a*) Ethyl oxoaristate (3·2 mg.) when hydrogenated in acetic acid in the presence of platinum absorbed 1·95 mols. of hydrogen.

(*b*) Ethyl oxoaristate (117 mg.) was hydrogenated in ethanol in presence of platinum. Evaporation of the solvent gave an almost colourless oil (115 mg.) (probably *ethyl tetrahydrooxoaristate*) [Found: equiv. (by hydrolysis), 281. $C_{17}H_{30}O_3$ requires equiv., 282]. Acidification of the hydrolysis liquors and extraction with light petroleum gave an acidic oil (75 mg.), $\lambda_{max.}$ 287 (ε, 51), which only partially crystallised after several weeks.

Methyl Oxoaristate.—Aristolactone (252 mg.) was dissolved in N-methanolic potassium hydroxide (2 ml.) and methanol (90%; 25 ml.); the product, isolated as above, yielded *methyl oxoaristate* (250 mg.) in needles, m. p. 68—69° (from aqueous ethanol), $[\alpha]_D^{14}$ +342° (*c*, 1·23), $\lambda_{max.}$ at 209 mμ (ε, 6360) and 290 mμ (ε, 264) (Found: C, 72·1; H, 9·1. $C_{16}H_{24}O_3$ requires C, 72·7; H, 9·1%). Infrared spectrum: peaks at 1650 (m) and 890 (s) (vinylidene), 840 (w), 800 (w), and 781 (w) (tetrasubstituted ethylene), 1735 and 1150—1200 (broad band) (ester carbonyl), 1720 (ketone), and 1100 cm.$^{-1}$ (*cyclo*hexanone derivative). Iodine value equivalent to 2·15 double bonds.

Hydrolysis. Methyl oxoaristate (162 mg.) was refluxed with ethanolic potassium hydroxide (0·66N; 5 ml.) (Found: equiv., 266. $C_{16}H_{24}O_3$ requires equiv., 264). The hydrolysis liquors were acidified, saturated with sodium chloride, and extracted with light petroleum yielding an extremely viscous oil (178 mg.).

Reactions of Aristolactone with Alcoholic Ammonia.—(*a*) Arisolactone (50 mg.) was dissolved in ethanol (95%; 5 ml.), and the solution was saturated with ammonia and set aside overnight. Concentration and dilution with water gave unchanged aristolactone, m. p. 107—109°.

(*b*) Aristolactone (74 mg.) was dissolved in ethanol (95%; 5 ml.), zinc dust (30 mg.) added, and the solution saturated with ammonia. The product isolated at the point of maximum optical rotation (after 3 days) was separated by concentration and dilution with water. Crystallisation from ethanol (70%) yielded needles of ethyl oxoaristate (35 mg.), m. p. 56—57° (Found: C, 73·8; H, 9·5. Calc. for $C_{17}H_{26}O_3$: C, 73·3; H, 9·3%).

(*c*) Aristolactone (30 mg.), when treated with *iso*propanol, ammonia, and zinc dust as in (*b*), was recovered unchanged.

(*d*) Aristolactone (70 mg.) when treated with methanolic ammonia in the presence of zinc dust as in (*b*) yielded methyl oxoaristate (26 mg.), m. p. 68—69° (from 70% *ethanol*), undepressed on admixture with a sample prepared from aristolactone and methanolic potassium hydroxide.

(*e*) Aristolactone (30 mg.), after treatment with triethylamine (0·5 ml.) in ethanol in the presence of zinc dust as in (*b*), was obtained unchanged.

iso*Aristolactone.*—Aristolactone (1 g.) in acetic acid (10 ml.) was heated for 12 hr. in an atmosphere of carbon dioxide at 130°. Removal of the solvent under reduced pressure gave a brown oil, which was dissolved in light petroleum, filtered from resinous material (0·1 g.), and washed with aqueous sodium hydrogen carbonate and then with water. Concentration and crystallisation gave iso*aristolactone* (0·15 g.), m. p. 90—91°, $[\alpha]_D^{17}$ −44° (*c*, 1·4), $\lambda_{max.}$ 209 mμ (ε, 11,200) and 272 mμ (ε, 640) (Found: C, 77·55; H, 8·7. $C_{15}H_{20}O_2$ requires C, 77·6; H, (8·6%). Infrared spectrum in carbon disulphide (0·5M): peaks at 892 (s) and 1655 (vinylidene) and 787 (m) and 842 cm.$^{-1}$ (m) (tetrasubstituted ethylene). Iodine value equivalent to 2·35 double bonds. A second crop of crystals (0·2 g.; m. p. 83—87°) and an oil (0·48 g.; $[\alpha]_D^{17}$ −38·1°) were also obtained. The latter was unchanged on further treatment with boiling acetic acid.

Attempted hydrolysis. *iso*Aristolactone (106 mg.) was refluxed with ethanolic potassium hydroxide (0·66N; 2 ml.) for 40 min. The solution was diluted and neutralised with 0·05N-sulphuric acid, giving *iso*aristolactone (46 mg.), m. p. and mixed m. p. 90—91°. The mother liquors were extracted with light petroleum, acidified, then re-extracted with light petroleum, and dried (Na_2SO_4), yielding an acidic oil.

Hydrogenation. (*a*) *iso*Aristolactone (140 mg.), when hydrogenated in ethanol in presence of platinum for 48 hr., absorbed 3·2 mols. of hydrogen, and yielded needles of hexahydroaristolactone, m. p. and mixed m. p. 102—104° [Found: equiv. (by hydrolysis), 242. Calc. for $C_{15}H_{26}O_2$: equiv., 238].

(*b*) *iso*Aristolactone (111 mg.) was hydrogenated for 10 min. in ethanol in presence of

platinum; 0·9 mol. of hydrogen was absorbed. Evaporation of the solvent gave needles of *dihydroaristolactone*, m. p. 79·5—80°, $[\alpha]^{17}$ −75°, $\lambda_{max.}$ 209 mμ (ε, 7800) and 271 mμ (ε, 606) (Found: C, 77·0; H, 9·5. $C_{15}H_{22}O_2$ requires C, 76·85; H, 9·5%). Infrared spectrum in carbon disulphide (0·5M): peaks at 894 (ms) and 1673 (w) (vinylidene ?), 1775 (s) (saturated γ-lactone), and 782 (m) and 840 (m) cm.$^{-1}$ (tetrasubstituted ethylene). A mixture with authentic dihydroaristolactone had m. p. 78—80°.

Ozonolysis of Aristolactone.—Aristolactone (0·5 g.) was ozonised at −30° in ethyl acetate for 30 min., and the product subsequently hydrogenated in the presence of platinum in the same solvent. Water-soluble products were extracted by being shaken with saturated aqueous sodium chloride. The water-insoluble fraction was concentrated and yielded a water-immiscible oil, which gave a positive reaction with Schiff's reagent and yielded an amorphous mixture of 2 : 4-dinitrophenylhydrazones. The aqueous distillate from the brine solution gave a positive Schiff's reaction for aldehydes, but no reaction for ketones. Formaldehyde was identified by oxidation with hydrogen peroxide to formic acid, the solution then giving a negative Schiff's reaction, but readily reducing mercuric chloride. Formaldehyde was confirmed by conversion into the dimedone derivative, m. p. and mixed m. p. 187—189°.

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THE SCHOOL OF PHARMACY, THE ROYAL TECHNICAL COLLEGE, GLASGOW. [*Received, January 3rd,* 1955.]

Triterpenoids. Part XXXV. The Reactions of* 12-Oxo*iso*ursa-9(11) : 14-*dien*-3β-*yl Acetate.*

By J. DOUGLAS EASTON and F. S. SPRING.

[Reprint Order No. 6083.]

The major product obtained by oxidation of 12-oxours-9(11)-en-3β-yl acetate (I) with selenium dioxide is shown to be correctly represented as 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate (II).

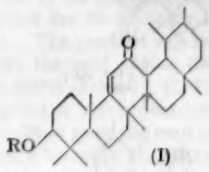
THE present paper describes an investigation of the reactions of 12-oxo*iso*-α-amyradien-3β-yl acetate, including its reduction. The investigation leads to the view that this compound is correctly represented as (II) and it will in future be named 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate, in conformity with practice in the oleanane series.

12-Oxours-9(11)-en-3β-yl acetate, represented as (I) † by Meisels, Jeger, and Ruzicka (*Helv. Chim. Acta*, 1950, **33**, 700), is oxidised by selenium dioxide to the diene (II) (Ruzicka, Rüegg, Volli, and Jeger, *ibid.*, 1947, **30**, 140; Meisels, Jeger, and Ruzicka, *loc. cit.*; Rüegg, Dreiding, Jeger, and Ruzicka, *ibid.*, 1950, **33**, 890). Ruzicka *et al.* (*loc. cit.*) reported that catalytic reduction of (II) under relatively mild conditions (room temperature, atmospheric pressure) regenerated 12-oxours-9(11)-en-3β-yl acetate (I) in high yield, together with a smaller quantity of ursa-9(11) : 12-dien-3β-yl acetate (III). This report led McLean, Ruff, and Spring (*J.*, 1951, 1093) to the view that (I) and (II) do not adequately express the relationship of 12-oxours-9(11)-en-3β-yl acetate and its oxidation product. In the meantime, an investigation of the analogous product obtained by oxidation of 12-oxo-olean-9(11)-en-3β-yl acetate has shown that it is (IV) [12-oxo*iso*oleana-9(11) : 14-dien-3β-yl acetate] (Allan, Johnston, and Spring, *J.*, 1954, 1546; Johnston and Spring, *J.*, 1954, 1556), a formula first advanced for it by Jeger and Ruzicka (*Helv. Chim. Acta*, 1945, **28**, 209). Similar treatment of 12-oxo*iso*oleana- and 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate gives the same degradation product (V) (Meisels, Jeger, and Ruzicka, *loc. cit.*), a behaviour which, with their parallel derivations, supports the structural relation implied by (II) and (IV). Two major differences in the behaviour of the oxo*iso*-dienyl acetates derived from α- and β-amyrin are to be noted. First, in contrast to the behaviour of the ursane analogue

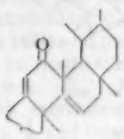
* Part XXXIV, *J.*, 1955, 1607.

† Configurations are not implied in the formulæ used in this paper; unless otherwise specified R = Ac.

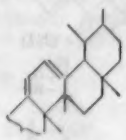
(II) described above, catalytic hydrogenation (hydrogenolysis) of 12-oxo*iso*olean-9(11) : 14-dien-3β-yl acetate (IV) leads to *neo*-β-amyrin which, as expected, has a different carbocyclic structure from that of β-amyrin and has been formulated as (VI; R = H) (Allan, Johnston, and Spring, *loc. cit.*). Secondly, the diene (IV) is stable to prolonged treatment with mineral acid (Budziarek, Johnston, Manson, and Spring, *J.*, 1951, 3019) whereas this treatment converts the analogue (II) into an isomer "12-oxo*iso*-α-amyradien-3β-yl-II acetate" (Ruzicka *et al.*, *loc. cit.*). The latter difference will be discussed in a later paper.



(I)



(II)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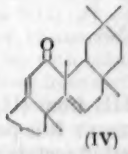

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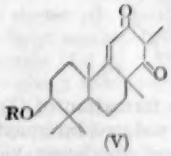
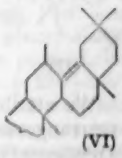
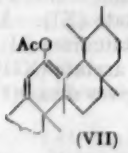


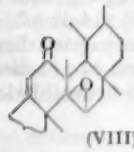
(V)


(VI)

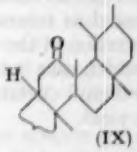
The product obtained by oxidation of the monoenyl acetate (I) with selenium dioxide is not homogeneous. Careful chromatography gave pure 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate, $[\alpha]_D$ +7°, characterised by hydrolysis to the corresponding alcohol, $[\alpha]_D$ −6°. Later fractions from the chromatogram are mixtures which could not be resolved into their components; they are almost certainly mixtures of 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate and "12-oxo*iso*-α-amyradien-3β-yl-II acetate," in varying proportions, since they are converted in high yield into pure "oxo-dienyl-II acetate" by treatment with hydrochloric acid.



(VII)



(VIII)

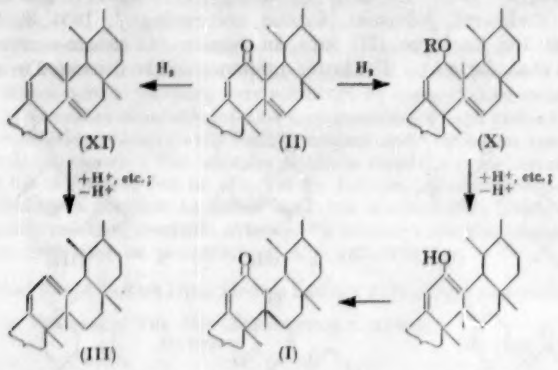


(IX)

12-Oxours-9(11)-en-3β-yl acetate (I) readily forms an enol acetate (VII) which shows the ultraviolet absorption spectrum and large dextrorotation associated with a 9(11) : 12-diene and is hydrolysed to 12-oxours-9(11)-en-3β-ol (I; R = H). As expected, 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate (II) is recovered unchanged after attempted enol-acetylation. Oxidation of the enol acetate (VII) with selenium dioxide gives a low yield of 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate (II) which with potassium permanganate gives, in high yield, a compound, $C_{32}H_{48}O_4$, which shows the ultraviolet absorption of an αβ-unsaturated ketone but, in contrast to (II), does not give a colour with tetranitromethane; it is provisionally represented as the 14 : 15-epoxide (VIII). The reactions of the α-amyrin derivatives described in this paragraph are exactly analogous to those of the corresponding β-amyrin derivatives (Budziarek *et al.*; Johnston and Spring, *locc. cit.*).

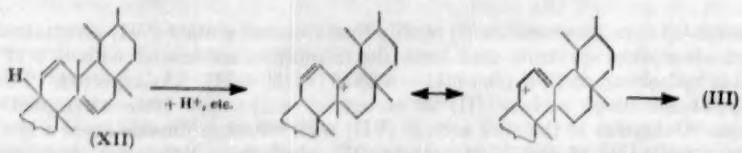
Hydrogenation of 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate (II), in our hands, gave products which were difficult to separate and varied considerably in nature with slight differences in the solvent. Two representative experiments are described in the Experimental section. In the first, with purified acetic acid as solvent, a mixture was obtained, chromatography of which gave 12-oxours-9(11)-en-3β-yl acetate (I) in maximum (crude) yield of 10%, the only other homogeneous product isolated being a saturated ketone (maximum crude yield, 27%), considered to be 12-oxo*iso*ursan-3β-yl acetate (IX). The

second experiment differed in that reduction was made in the presence of a trace of hydrochloric acid: 12-oxours-9(11)-en-3β-yl acetate was then isolated in considerably greater yield (maximum, crude, 36%) and, in addition, impure ursa-9(11):12-dien-3β-yl acetate



(III) in high yield. We attribute the formation of (I) and (III) from (II) to the great facility with which rearrangement of a reduced intermediate occurs; it is pertinent to our argument that (II) is recovered unchanged after being shaken in ethyl acetate with hydrogen and platinum. The formation of (I) and (III) from (II) is represented as annexed. Supporting evidence is presented below. Reduction of 12-oxo*iso*ursa-9(11):14-dien-3β-yl acetate with lithium aluminium hydride, or with sodium and pentyl alcohol, followed by acetylation of the products, gave *iso*ursa-9(11):14-diene-3β:12-diol diacetate (X) in good yield and this with hydrochloric acid in acetic acid or with hydrogen chloride in chloroform gave, in low yield, 12-oxours-9(11)-en-3β-yl acetate (I).

Reduction of 12-oxo*iso*ursa-9(11):14-dien-3β-yl acetate (II) by the Wolff–Kishner method gives, in good yield, a non-conjugated dienyl acetate. This does not show selective absorption above 2200 Å but shows strong ethylenic absorption between 2000 and 2230 Å and may be represented as *iso*ursa-9(11):14-dien-3β-yl acetate (XI). Alternatively it is possible that the formation of the non-conjugated dienyl acetate from (II) includes double-bond movement in which case it is *iso*ursa-11:14-dien-3β-yl acetate (XII). Treatment of this non-conjugated dienyl acetate with hydrochloric acid gives ursa-9(11):12-dien-3β-yl acetate (III) in high yield.



The fact that the non-conjugated dienyl acetate cannot be hydrogenated does not exclude formulation (XII). Wolff–Kishner reduction of 12-oxo*iso*oleana-9(11):14-dien-3β-yl acetate gives two isomeric non-conjugated dienyl acetates, one of which has a constitution corresponding to (XI), the other being the *iso*oleanane analogue of (XII) (Allan, Johnston, and Spring, *loc. cit.*). Neither of these is changed when shaken in acetic acid with platinum and hydrogen. Whereas the isomer corresponding to (XI) readily isomerises to oleana-9(11):12-dien-3β-yl acetate when treated with mineral acid, similar treatment of the 11:14-dienyl acetate gives the 11:13(18)-diene acetate. This behaviour appears to support formula (XI) for the *iso*ursane non-conjugated dienyl acetate. In our view, this argument by analogy is not valid, because of the extreme difficulty encountered in the formation of ursa-11:13(18)-dien-3β-yl acetate from α-amyrin acetate by methods which lead to the formation, in high yield, of oleana-11:13(18)-dien-3β-yl acetate from β-amyrin

acetate (Easton, Manson, and Spring, *J.*, 1953, 943); the conversion of (XII) into ursa-9(11) : 12-dien-3β-yl acetate may be represented as above.

Experimental

Specific rotations were measured in $CHCl_3$ solution at room temperature, and ultraviolet absorption spectra in EtOH. Grade II alumina and light petroleum, b. p. 60—80°, were used for chromatography.

Enol Acetate of 12-*Oxours*-9(11)-*en*-3β-*yl Acetate*.—12-Oxours-9(11)-en-3β-yl acetate (790 mg.) was refluxed for 60 hr. with acetic anhydride (60 c.c.) containing freshly fused sodium acetate (1·2 g.). The product was isolated in the usual manner and crystallised from methanol–benzene to give the *enol acetate* (500 mg.) as needles, m. p. 257—258°, $[\alpha]_D$ +231° (*c*, 0·5), $\lambda_{max.}$ 2780 Å (ε 9000) (Found: C, 77·9; H, 9·9. $C_{34}H_{52}O_4$ requires C, 77·8; H, 9·9%). The enol acetate gives a red-brown colour with tetranitromethane. Similar treatment of 12-oxours-9(11)-en-3β-ol gave the enol acetate, m. p. and mixed m. p. 257—258°. The enol acetate was refluxed for 2 hr. with 3% ethanolic potassium hydroxide to yield 12-oxours-9(11)-en-3β-ol as needles (from aqueous methanol), m. p. and mixed m. p. 238—240°, $[\alpha]_D$ +77° (*c*, 0·6).

12-*Oxoisoursa*-9(11) : 14-*dien*-3β-*yl Acetate* (cf. Ruzicka, Rüegg, Volli, and Jeger, *loc. cit.*).—(*a*) A solution of 12-oxours-9(11)-en-3β-yl acetate (2·0 g.) in glacial acetic acid (65 c.c.) was refluxed for 24 hr. with selenium dioxide (3·0 g.). The crude product, isolated in the usual manner, crystallised from methanol to give a solid (600 mg.), m. p. 226—229°, $[\alpha]_D$ +26° (*c*, 2·0). A solution of the solid in benzene–light petroleum (1 : 4; 100 c.c.) was chromatographed on a column (8 × 2 cm.) of alumina, and the fraction eluted with the same solvent mixture (1 : 4, 500 c.c.; 1 : 2, 200 c.c.) was repeatedly crystallised from chloroform–methanol to yield 12-oxo-*iso*ursa-9(11) : 14-dien-3β-yl acetate as needles, m. p. 221—222°, $[\alpha]_D$ +7°, +8°, (*c*, 0·5; 1·1), $\lambda_{max.}$ 2100 and 2370 Å (ε 6100, 11,000) (Found: C, 79·8; H, 10·3. Calc. for $C_{32}H_{48}O_3$: C, 79·95; H, 10·1%). The second fraction {150 mg.; m. p. 228—230°, $[\alpha]_D$ +19° (*c*, 0·9)} and the third fraction {70 mg.; m. p. 250—253°, $[\alpha]_D$ +99° (*c*, 2·9)} from the column could not be purified by crystallisation and on treatment with hydrogen chloride in acetic acid [as described by Ruzicka, Rüegg, Volli, and Jeger, *loc. cit.*, for 12-oxo*iso*ursa-9(11)-14-dien-3β-yl acetate] gave the "oxo*iso*-dienyl-II acetate," m. p. 269—271°, $[\alpha]_D$ +157° (*c*, 2·0), in high yield.

(*b*) A solution of the enol acetate from 12-oxours-9(11)-en-3β-yl acetate (500 mg.) in glacial acetic acid (60 c.c.) was heated under reflux for 24 hr. with selenium dioxide (1·5 g.). The product was isolated in the usual way and fractionally crystallised from chloroform–methanol. The first three fractions were combined and recrystallised to give starting material (250 mg.; m. p. and mixed m. p.). The fourth and fifth crops differed from the first three in giving a yellow colour with tetranitromethane. They were combined and crystallised four times from chloroform–methanol to yield 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate as needles, m. p. and mixed m. p. 219—220°.

12-*Oxoisoursa*-9(11) : 14-*dien*-3β-*ol* was obtained from the acetate by using 3% ethanolic potassium hydroxide. It separates from *n*-hexane–acetone as needles, m. p. 116—119°, $[\alpha]_D$ −6°, −6° (*c*, 1·6, 1·8) (Found: C, 81·9; H, 10·7. $C_{30}H_{46}O_2$ requires C, 82·1; H, 10·6%). Treatment of the alcohol with pyridine and acetic anhydride regenerated the acetate, m. p. 220—221°, $[\alpha]_D$ +7° (*c*, 1·4).

Oxidation of 12-*Oxo*isoursa-9(11) : 14-*dien*-3β-*yl Acetate with Potassium Permanganate*.—A stirred solution of the oxo-dienyl acetate (0·5 g.) in stabilised glacial acetic acid (200 c.c.) was treated during 30 min. with a solution of potassium permanganate (132 mg.) in water (20 c.c.). Stirring was continued for 30 min. and the product isolated in the usual manner. Crystallisation from chloroform–methanol gave 14 : 15-*epoxy*-12-*oxo*isours-9(11)-*en*-3β-*yl acetate* as needles (300 mg.), m. p. 280—283°, $[\alpha]_D$ +56°, +55° (*c*, 1·2, 0·9), $\lambda_{max.}$ 2400 Å (ε 8100) (Found: C, 77·5; H, 9·8. $C_{32}H_{48}O_4$ requires C, 77·4; H, 9·7%). It does not give a colour with tetranitromethane.

Catalytic Hydrogenation of 12-*Oxoisoursa*-9(11) : 14-*dien*-3β-*yl Acetate*.—(*a*) The oxo-dienyl acetate (1·0 g.) in glacial acetic acid was shaken with platinum (from 300 mg. of PtO_2) and hydrogen for 20 hr. The product, isolated in the usual way, was chromatographed in benzene–light petroleum (1 : 2; 225 c.c.) on alumina (12 × 1·5 cm.). The fraction (750 mg.) eluted with the same solvent mixture (800 c.c.) had m. p. 207—240°. Washing with benzene–light petroleum (2 : 1; 200 c.c.) and benzene (200 c.c.) gave a fraction (100 mg.), repeated crystallisation of which from chloroform–methanol gave 12-oxours-9(11)-en-3β-yl acetate (59 mg.) as plates, m. p. and mixed m. p. 285—288°, $[\alpha]_D$ +82° (*c*, 1·3), $\lambda_{max.}$ 2520 Å (ε 10,300). A third

fraction (80 mg.), obtained by washing with benzene–ether (19 : 1; 400 c.c.), separated from chloroform–methanol as plates, m. p. 212—251°, and was not further examined.

The first fraction, from the chromatogram described above, in benzene–light petroleum (1 : 5; 220 c.c.) was re-chromatographed on alumina (10 × 2 cm.), and the column washed with benzene–light petroleum (1 : 5, 800 c.c.; 1 : 2, 400 c.c.) to yield a fraction (120 mg.), m. p. 176—190°. A fraction B (270 mg.) obtained by washing with benzene–light petroleum (2 : 1; 800 c.c.), benzene (400 c.c.), and ether–benzene (1 : 19; 200 c.c.) separated from chloroform–methanol as plates, m. p. 207—210°. Later fractions had spread m. p.s and were not examined. Fraction B, in light petroleum (170 c.c.), was again chromatographed on alumina (11 × 1 cm.), and the column washed with the same solvent giving a fraction (36 mg.). Washing with benzene–light petroleum (1 : 19; 300 c.c.) gave a second fraction (70 mg.) which was crystallised from chloroform–methanol to yield *12-oxoisoursan-3β-yl acetate* as plates, m. p. 222—223°, $[\alpha]_D$ +93°, +91° (*c*, 0·9, 1·1), $\lambda_{max.}$ 2890 Å (ε 63) (Found: C, 79·3; H, 10·9. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). The ketone does not give a colour with tetranitromethane.

(*b*) A solution of 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate (1 g.) in glacial acetic acid was hydrogenated as described above with the difference that 1 drop of concentrated hydrochloric acid was added to the solution. The dried product in benzene–light petroleum (1 : 4; 100 c.c.) was chromatographed on alumina (12 × 2 cm.). Washing with benzene–light petroleum mixtures (1 : 4, 600 c.c.; 1 : 1, 450 c.c.) and benzene (300 c.c.) gave a fraction (420 mg.) crystallisation of which from chloroform–methanol gave needles, m. p. 178—179°, $[\alpha]_D$ +262° (*c*, 0·8), $\lambda_{max.}$ 2800 Å (ε 6900). This fraction, which gives a red-brown colour with tetranitromethane, is impure ursa-9(11) : 12-dien-3β-yl acetate; a mixture with the pure dienyl acetate had an intermediate m. p. The column was next washed with ether–benzene (1 : 19, 450 c.c.; 1 : 2, 300 c.c.; 2 : 1, 150 c.c.) to yield a fraction (360 mg.) crystallisation of which from chloroform–methanol yielded 12-oxours-9(11)-en-3β-yl acetate (156 mg.), m. p. and mixed m. p. 280—283°, $[\alpha]_D$ +89° (*c*, 1·0), $\lambda_{max.}$ 2480 Å (ε 9600).

Reduction of 12-*Oxoisoursa*-9(11) : 14-*dien*-3β-*yl Acetate with Lithium Aluminium Hydride.*—A solution of the oxo-dienyl acetate (0·5 g.) in dry ether (150 c.c.) was refluxed for 4 hr. with lithium aluminium hydride (0·5 g.). The product was isolated in the usual manner (avoiding the use of acid) and acetylated by heating it with pyridine and acetic anhydride. The acetylated product was repeatedly crystallised from methanol to yield *iso*ursa-9(11) : 14-*diene*-3β : 12-*diol diacetate* as plates, m. p. 194—195°, $[\alpha]_D$ +59°, +60° (*c*, 1·9, 1·5) (Found C, 78·2; H, 10·1. $C_{34}H_{52}O_4$ requires C, 77·8; H, 10·0%). Light absorption: $\varepsilon_{2100} = 7000$, $\varepsilon_{2150} = 5200$, $\varepsilon_{2200} = 2400$. The diacetate gives a yellow colour with tetranitromethane.

Reduction of 12-*Oxoisoursa*-9(11) : 14-*dien*-3β-*yl Acetate with Sodium and Pentyl Alcohol.*—A solution of the oxo-dienyl acetate (500 mg.) in boiling pentyl alcohol (20 c.c.) was treated with sodium (1·2 g.), and the mixture refluxed for 30 min. Pentyl alcohol (3·3 c.c.) was added and refluxing continued for 40 min. The product was isolated in the usual manner and boiled for 2 hr. with acetic anhydride (20 c.c.). The acetylated product was chromatographed on alumina to yield an easily eluted fraction (290 mg.) which crystallised from methanol and was purified by recrystallisation from chloroform–methanol to yield *iso*ursa-9(11) : 14-diene-3β : 12-diol diacetate (192 mg.) as plates, m. p. and mixed m. p. 193—194, $[\alpha]_D$ +58° (*c*, 2·0) (Found: 78·1; H, 10·0%).

Treatment of iso*Ursa*-9(11) : 14-*diene*-3β : 12-*diol Diacetate with Hydrochloric Acid.*—A solution of the diacetate (300 mg.) in acetic acid (30 c.c.) was treated with concentrated hydrochloric acid (1·5 c.c.), and the mixture kept at 90° for 15 min. and then at room temperature overnight. The product was isolated in the usual manner and acetylated by pyridine–acetic anhydride. The acetylated product was chromatographed on alumina to give readily eluted fractions (180 mg.) which could not be crystallised. Thereafter, ether–benzene (1 : 19) eluted a fraction (20 mg.) which on crystallisation from chloroform–methanol yielded 12-oxours-9(11)-en-3β-yl acetate as plates, m. p. and mixed m. p. 286—289°, $[\alpha]_D$ +83° (*c*, 0·7), $\lambda_{max.}$ 2480 Å (ε 10,700). The same product was obtained in approximately the same yield by treatment of the diacetate (260 mg.) in chloroform (30 c.c.) with dry hydrogen chloride for 1 hr., the mixture being kept at room temperature for 4 days.

Wolff–Kishner Reduction of 12-*Oxoisoursa*-9(11) : 14-*dien*-3β-*yl Acetate.*—A mixture of the oxo-dienyl acetate (2·0 g.), 100% hydrazine hydrate (10 c.c.), sodium methoxide (from 2·0 g. of sodium), and methanol (25 c.c.) was kept at 200° for 13 hr. in an autoclave. The product was acetylated by pyridine and acetic anhydride and crystallised from methanol and then repeatedly from methanol–chloroform to yield *iso*ursa-x : 14-*dien*-3β-*yl acetate* as needles, m. p. 171—172°, $[\alpha]_D$ +43°, +42° (*c*, 1·3, 1·0) (Found: C, 8·26; H, 11·0. $C_{32}H_{50}O_2$ requires C, 82·3; H, 10·8%).

Light absorption: $\varepsilon_{2100} = 6900$, $\varepsilon_{2150} = 4100$, $\varepsilon_{2200} = 1500$, $\varepsilon_{2230} = 700$. The dienyl acetate gives a strong yellow colour with tetranitromethane. The dienyl acetate (150 mg.) was recovered unchanged after shaking of its solution in ethyl acetate–glacial acetic acid with hydrogen and platinum for 17 hr.

Conversion of iso*Ursa*-x : **14-*dien*-3β-*yl Acetate into Ursa*-9(11) : 12-*dien*-3β-*yl Acetate*.**—A solution of *iso*ursa-*x* : 14-dien-3β-yl acetate (100 mg.) in dry chloroform (20 c.c.) was treated with a stream of dry hydrogen chloride for 45 min. and then kept at room temperature for 5 days. The mixture was evaporated and the residue crystallised from chloroform–methanol to yield ursa-9(11) : 12-dien-3β-yl acetate as needles, m. p. and mixed m. p. 168—169°, $[\alpha]_D$ +320° (c, 1·0), $\lambda_{max.}$ 2820 Å (ε 9200) (Found: C, 82·2; H, 11·2. Calc for $C_{32}H_{50}O_2$: C, 82·3; H, 10·8%).

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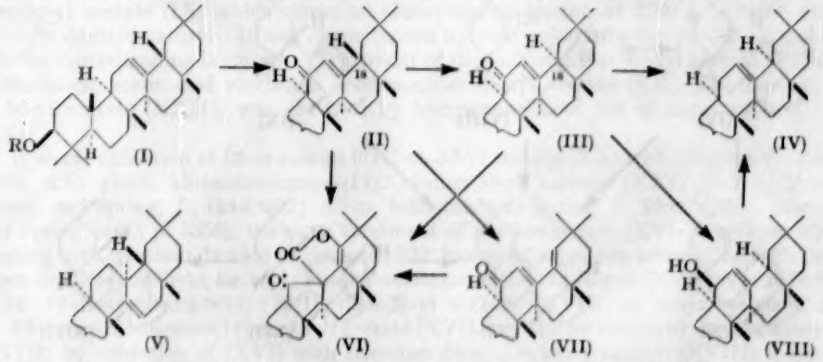
Triterpenoids. Part XXXVI. Reactions of* 18α-*Olean*-12-*en*-3β-*ol Derivatives and Observations on the Stereochemistry of* α-*Amyrin.*

By G. G. ALLAN and F. S. SPRING.

[Reprint Order No. 6084.]

The reactions of 18α-olean-12-en-3β-ol (IV; R = H) are compared with those of its 18β-isomer, β-amyrin (I; R = H). A comparison of the properties of 12-oxo-18α-olean-9(11)-en-3β-yl acetate (XVI), 12-oxo-olean-9(11)-en-3β-yl acetate (XX), and 12-oxours-9(11)-en-3β-yl acetate leads to the view that the stereochemistry of the last compound is as shown in (XXIV), *i.e.*, that rings D and E in α-amyrin are *cis*-β-fused.

FOUR of the five oleanen-3β-ols containing the double bond in the 9 : 11 : 12 : 13 : 18 : 19 fragment are known Olean-18-en-3β-ol is the naturally occurring germanicol (Barton and Brooks, *J.*, 1951, 251); olean-13(18)-en-3β-ol has been prepared from β-amyrin (Jeger and Ruzicka, *Helv. Chim. Acta*, 1941, **24**, 1243; Ruzicka, Jeger, and Norymberski, *ibid.*, 1942, **25**, 457) and from lupeol (Ames, Halsall, and Jones, *J.*, 1951, 450) and it has been isolated from a natural source (Musgrave, Stark, and Spring, *J.*, 1952, 4393). Olean-9(11)-en-3β-ol has been prepared from β-amyrin (Jeger and Ruzicka, *Helv. Chim. Acta*, 1945, **28**,



209; Budziarek, Johnston, Manson, and Spring, *J.*, 1951, 3019) and olean-12-en-3β-ol (I; R = H)† is the naturally occurring β-amyrin.

One stereoisomer of the four unsaturated alcohols named above had been described when the present investigation was commenced. This is 18α-olean-12-en-3 β-ol (IV; R = H),

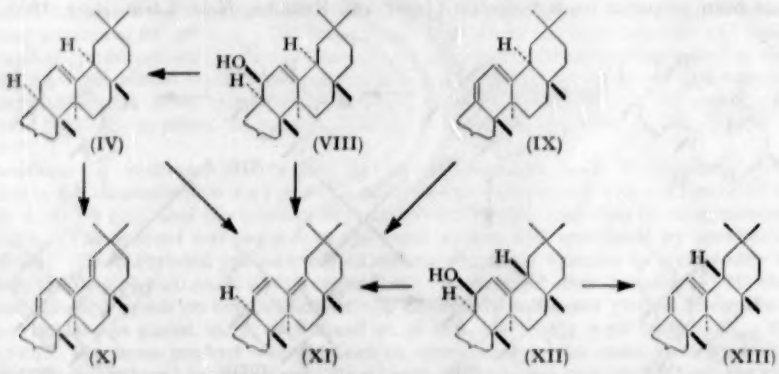
* Part XXXV, preceding paper. † Throughout this paper R = Ac unless otherwise stated.

prepared by Budziarek, Manson, and Spring (*J.*, 1951, 3336) by treatment of 11-oxo-olean-12-en-3β-yl benzoate (II; R = Bz) with concentrated alkali, which furnished 11-oxo-18α-olean-12-en-3β-ol (III; R = H), the acetate of which was then hydrogenated. Taraxerol, formulated as 13α-olean-18-en-3β-ol by Brooks (*Chem. and Ind.*, 1953, 1178), has since been shown to be *iso*olean-14-en-3β-ol (V; R = H) (Beaton, Spring, Stevenson, and Stewart, *Chem. and Ind.*, 1954, 1454; 1955, 35).

The investigation of 18α-olean-12-en-3β-ol described in this paper was undertaken with the object of comparing it with α-amyrin in the hope that the comparison would disclose the stereochemistry of the D–E ring junction in the ursane group of triterpenoids. In our view, this objective has been achieved.

11-Oxo-18α-olean-12-en-3β-yl acetate (III) resembles its 18β-isomer (II) in that on oxidation with selenium dioxide it yields the "O_6-acetate" recently identified as the enol lactone (VI) (McKean and Spring, *J.*, 1954, 1989). It is probable that the formation of the enol lactone from (II) proceeds *via* 11-oxo-oleana-12 : 18-dien-3β-yl acetate (VII) which is readily obtained from (II) by treatment with bromine (Picard and Spring, *J.*, 1941, 35) and on oxidation with selenium dioxide gives the enol lactone (VI) (McKean and Spring, *loc. cit.*). The 18α-isomer (III), however, is recovered unchanged after treatment with bromine in conditions which lead to the formation of (VII) from (II).

Reduction of 11-oxo-18α-olean-12-en-3β-yl acetate (III) with lithium aluminium hydride, followed by acetylation of the product, yields 11β-hydroxy-18α-olean-12-en-3β-yl acetate (VIII); to the hydroxyl group in (VIII) is ascribed the β(axial)-configuration because of its hindered character. 11β-Hydroxyolean-12-en-3β-yl acetate (XII) [the 18β-isomer of (VIII); Allan, Johnston, and Spring *J.*, 1954, 1546] is smoothly dehydrated by treatment with acetic anhydride and sodium acetate, to oleana-9(11) : 12-dien-3β-yl acetate (XIII). Similar treatment of the 18α-compound (VIII), however, gives mixed crystals of 18α-oleana-9(11) : 12-dien-3β-yl acetate (IX) and oleana-11 : 13(18)-dien-3β-yl acetate (XI); the specific rotation and ultraviolet absorption spectrum of these show that they contain approximately 70% of the heteroannular and 30% of the homoannular dienyl acetate. Similar mixed crystals were obtained by refluxing 11β-hydroxy-18α-olean-12-en-3β-yl acetate with dimethylaniline; in neither case was it possible to separate the crystals into their components. Treatment with hydrochloric acid in acetic acid converted the mixture into the pure heteroannular dienyl acetate (XI) and this was obtained directly from (VIII) by treatment with the same acid mixture.

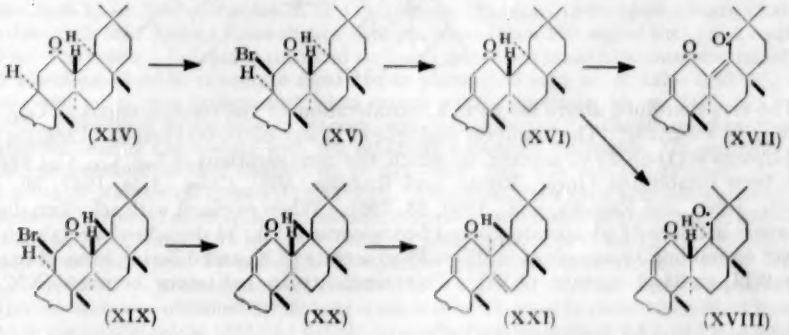


18α-Olean-12-en-3β-yl acetate (IV) was obtained by the method of Budziarek, Manson, and Spring (*loc. cit.*) and by hydrogenolysis of 11β-hydroxy-18α-olean-12-en-3β-yl acetate (VIII); it was characterised by hydrolysis to 18α-olean-12-en-3β-ol and by the preparation of esters. Oxidation of 18α-olean-12-en-3β-yl acetate (IV) with selenium dioxide or with *N*-bromosuccinimide proceeds in the same way as that of the 18β-isomer, β-amyrin acetate, giving (in similar conditions) oleana-11 : 13(18)-dien-3β-yl acetate (XI) (Budziarek,

Manson, and Spring, *loc. cit.*) and oleana-9(11) : 12 : 18-trien-3β-yl acetate (X) (Ruzicka, Jeger and Redel, *Helv. Chim. Acta*, **1943**, **26**, 1235) respectively.

12-Oxo-18α-oleanan-3β-yl acetate (XIV) and its 11-bromo-derivative (XV) were prepared by improved methods (cf. Budziarek, Manson, and Spring, *loc. cit.*). An examination of the infrared absorption spectrum of the bromo-ketone, kindly made by Dr. G. Eglinton, shows that the bromine atom is axial (β). In spite of the fact that the geometry of (XV) favours easy elimination of hydrogen bromide, the bromo-ketone proved to be very stable. This behaviour is to be contrasted with the ease of dehydrobromination of the 18β-relative, (XIX; R = Bz), which is converted into 12-oxo-olean-9(11)-en-3β-yl benzoate (XX; R = Bz) by hydrogen bromide in warm acetic acid (Seymour and Spring, *J.*, **1941**, 319); under these conditions the bromide (XV) is unchanged (Budziarek, Manson, and Spring, *loc. cit.*). Dehydrobromination of (XV), by prolonged refluxing with pyridine, gave 12-oxo-18α-olean-9(11)-en-3β-yl acetate (XVI) which shows the ultraviolet absorption of an αβ-unsaturated ketone and was characterised by the preparation of the related alcohol and benzoate.

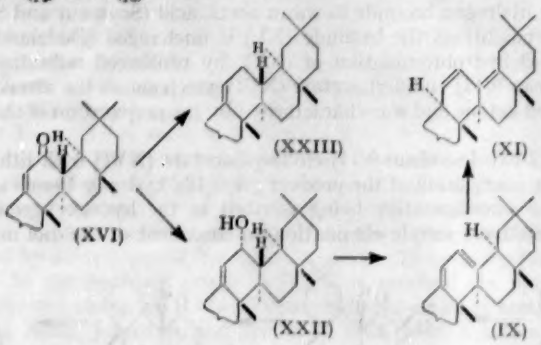
Reduction of 12-oxo-18α-olean-9(11)-en-3β-yl acetate (XVI) with lithium aluminium hydride followed by acetylation of the product gives 12α-hydroxy-18α-olean-9(11)-en-3β-yl acetate (XXII), the α-configuration being ascribed to the hydroxyl group because of its inertness and its relatively simple elimination on treatment of the diol monoacetate with



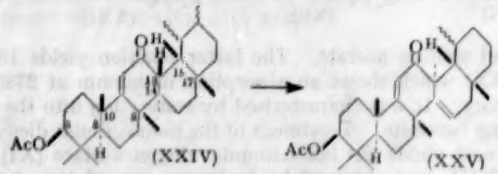
acetic anhydride and sodium acetate. The latter reaction yields 18α-oleana-9(11) : 12-dien-3β-yl acetate (IX) which shows an absorption maximum at 2780 Å (ε 9400) and is strongly dextrorotatory. It was characterised by conversion into the parent alcohol and into the corresponding benzoate. Treatment of the homoannular dienyl acetate (IX) with hydrochloric–acetic acid yields the heteroannular dienyl acetate (XI). 18α-Olean-9(11)-en-3β-yl acetate (XXIII) was obtained by hydrogenation of the αβ-unsaturated ketone (XVI).

Whereas oxidation of 12-oxo-olean-9(11)-en-3β-yl acetate (XX) with selenium dioxide in acetic acid yields 12-oxo*iso*oleana-9(11) : 14-dien-3β-yl acetate (XXI) (Green, Mower, Picard, and Spring, *J.*, **1944**, **527**; Allan, Johnston, and Spring, *J.*, **1954**, **1546**; Johnston and Spring, *ibid.*, p. 1556), the same treatment of the 18α-isomer (XVI) is without effect. Heating with selenium dioxide in dioxan at 200° has no effect on the ketone (XX) (Ruzicka, Jeger, and Norymberski, *loc. cit.*); similar oxidation of the 18α-isomer (XVI) gives a mixture of 12 : 19-dioxo-oleana-9(11) : 13(18)-dien-3β-yl acetate (XVII), as major product, and 12 : 19-dioxo-18α-olean-9(11)-en-3β-yl acetate (XVIII). The formation of the 18α-diketone (XVIII) by oxidation of (XVI) with selenium dioxide is remarkable; (XVIII) is not an intermediate in the oxidation of (XVI) to (XVII) since the 18α-diketone is recovered unchanged after treatment with selenium dioxide in dioxan at 200°. We attribute its formation to a reduction of the dioxo-dienyl acetate (XVII), the reducing agent being 12-oxo-18α-olean-9(11)-en-3β-yl acetate (XVI) which is thereby oxidised to 12-oxo-oleana-9(11) : 13(18)-dien-3β-yl acetate and then further oxidised to the dioxo-dienyl acetate (XVII) by selenium dioxide. The last stage in this reaction sequence has been described

(Beaton, Johnston, McKean, and Spring *J.*, 1953, 3660). The difference in behaviour between the isomers (XVI) and (XX) suggests that the formation of an *iso*oleanane derivative requires specific relative configurations at $C_{(13)}$, $C_{(14)}$, and $C_{(18)}$. The configurations at these centres in 12-oxo-olean-9(11)-en-3β-yl acetate (XX) permit a synchronous reaction, including the removal of the 13-hydrogen (β) and leading to a favourable conformation in the resulting 12-oxo*iso*oleana-9(11) : 14-dien-3β-yl acetate (XXI) in which the 13-methyl group (α) and the 18-hydrogen atom (β) are *anti*-related. This path is not open to 12-oxo-18α-olean-9(11)-en-3β-yl acetate (XVI) because of the unfavourable relative configurations at $C_{(14)}$ and $C_{(18)}$.



The views outlined above led us to a consideration of the configurations at $C_{(14)}$, $C_{(17)}$, and $C_{(18)}$ in α-amyrin. The α-amyrin analogue of 12-oxo-olean-9(11)-en-3β-yl acetate (XX) is 12-oxours-9(11)-en-3β-yl acetate, in which the configurations at $C_{(3)}$, $C_{(5)}$, $C_{(8)}$, and $C_{(10)}$ have been established (Jeger, Rüegg, and Ruzicka, *Helv. Chim. Acta*, 1947, **30**, 1294; Meisels, Jeger, and Ruzicka, *ibid.*, 1950, **33**, 700). When oxidised with selenium dioxide, 12-oxours-9(11)-en-3β-yl acetate gives 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate, in this respect resembling 12-oxo-olean-9(11)-en-3β-yl acetate (XX) and differing from 12-oxo-18α-olean-9(11)-en-3β-yl acetate (XVI). This similarity in behaviour between (XX) and



12-oxours-9(11)-en-3β-yl acetate and that between *iso*oleana-9(11) : 14-dien-3β-yl acetate and *iso*ursa-*x* : 14-dien-3β-yl acetate with mineral acid (see preceding paper) are best explained by assuming identical configurations at $C_{(13)}$, $C_{(14)}$, $C_{(17)}$, and $C_{(18)}$ in the two αβ-unsaturated ketones. We therefore represent the steric structure of 12-oxours-9(11)-en-3β-yl acetate as (XXIV) and that of 12-oxo*iso*ursa-9(11) : 14-dien-3β-yl acetate as (XXV). As a corollary rings D and E in α-amyrin are *cis*-β-fused, a conclusion also reached by Corey and Ursprung (*Chem. and Ind.* 1954, 1387; cf. Jeger, *Angew. Chem.*, 1951, **63**, 196; Ruzicka, *Experientia*, 1953, **9**, 357; Beton and Halsall, *Chem. and Ind.*, 1954, 1560; Zürcher, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1954, **37**, 2145).

Experimental

Specific rotations were measured in chloroform solution at room temperature and ultraviolet absorption spectra in ethanol.

11-Oxo-18α-olean-12-en-3β-yl Benzoate.—11-Oxo-18α-olean-12-en-3β-ol (Budziarek, Manson, and Spring, *loc. cit.*; m. p. 254—255°, $[\alpha]_D$ + 84°) was treated with benzoyl chloride and pyridine and the product crystallised from chloroform–methanol to give *11-oxo-18α-olean-12-en-3β-yl*

benzoate as plates, m. p. 263—264°, $[\alpha]_D$ +86° (*c*, 1·8) (Found: C, 81·2; H, 9·6. $C_{37}H_{52}O_3$ requires C, 81·6; H, 9·6%).

Oxidation of 11-*Oxo*-18α-*olean*-12-*en*-3β-*yl Acetate with Selenium Dioxide.*—A solution of the acetate (0·5 g.) in glacial acetic acid (20 c.c.) was refluxed with selenium dioxide (0·5 g.) for 20 hr. The product, isolated in the usual manner, crystallised from methanol to give the "$O_{(5)}$-acetate" as needles (300 mg.), m. p. 255—257°, $[\alpha]_D$ +33° (*c*, 1·1), undepressed in m. p. when mixed with an authentic specimen (Found: C, 75·1; H, 9·0. Calc. for $C_{32}H_{46}O_5$: C, 75·3; H, 9·1%).

11β-*Hydroxy*-18α-*olean*-12-*en*-3β-*yl Acetate.*—A solution of 11-oxo-18α-olean-12-en-3β-yl acetate (4 g.) in ether (500 c.c.) was heated under reflux with lithium aluminium hydride (2 g.) for 2 hr. The reaction product was treated with acetic anhydride and pyridine for 1 hr. on the water-bath. The acetylated product was isolated in the usual manner and crystallised from chloroform–methanol, to give 11β-*hydroxy*-18α-*olean*-12-*en*-3β-*yl acetate* (3·5 g.) as needles, m. p. 238—239°, $[\alpha]_D$ +46° (*c*, 1·3) (Found: C, 79·4; H, 11·0. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). Light absorption: $\varepsilon_{2960} = 5600$.

Treatment of 11β-*Hydroxy*-18α-*olean*-12-*en*-3β-*yl Acetate with Hydrochloric Acid.*—A solution of the diol monoacetate (270 mg.) in glacial acetic acid (150 c.c.) was treated with concentrated hydrochloric acid (1 c.c.) and heated on the steam-bath for 72 hr. The product, crystallised from chloroform–methanol, yielded oleana-11 : 13(18)-dienyl acetate (150 mg.), m. p. and mixed m. p. 227—228°, $[\alpha]_D$ −63° (*c*, 1·1), $\lambda_{max.}$ 2420, 2500, and 2600 Å (ε 27,000, 29,000, and 20,000) (Found: C, 82·4; H, 10·9. Calc. for $C_{32}H_{50}O_2$: C, 82·3; H, 10·8%).

18α-*Olean*-12-*en*-3β-*ol.*—A solution of 11β-hydroxy-18α-olean-12-en-3β-yl acetate (200 mg.) in glacial acetic acid (150 c.c.) was shaken with platinum (from 100 mg. of PtO_2) and hydrogen for 16 hr. The product, isolated in the usual manner, crystallised from chloroform–methanol from which 18α-olean-12-en-3β-yl acetate separated as plates (150 mg.), m. p. 243—244°, $[\alpha]_D$ +50° (*c*, 0·8); the m. p. was undepressed when mixed with a specimen (m. p. 246°, $[\alpha]_D$ +53°) prepared as described by Budziarek, Manson, and Spring (*loc. cit.*). 18α-*Olean*-12-*en*-3β-*ol* was prepared by heating the acetate with 5% ethanolic potassium hydroxide. It separates from chloroform–methanol as long needles, m. p. 213—214°, $[\alpha]_D$ +50° (*c*, 1·9) (Found: C, 84·3; H, 11·9. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). 18α-*Olean*-12-*en*-3β-*yl benzoate*, obtained from the alcohol in the usual manner, separates from chloroform–methanol as plates, m. p. 223—225°, $[\alpha]_D$ +64° (*c*, 3·5) (Found: C, 83·4; H, 10·4. $C_{37}H_{54}O_2$ requires C, 83·7; H, 10·3%). The benzoate was hydrolysed by boiling 10% ethanolic potassium hydroxide for 16 hr. to 18α-olean-12-en-3β-ol, m. p. and mixed m. p. 212—214°, $[\alpha]_D$ +49° (*c*, 1·2). 18α-*Olean*-12-*en*-3β-*yl hexahydrobenzoate* was obtained by shaking a solution of 11-oxo-18α-olean-12-en-3β-yl benzoate (0·8 g.) in glacial acetic acid (300 c.c.) with hydrogen and platinum (from 0·3 g. of PtO_2) for 48 hr. The product separated as plates after 30 hr.; it was isolated in the usual manner and crystallised from chloroform–methanol as plates (600 mg.), m. p. 210—211°, $[\alpha]_D$ +48° (*c*, 2·3) (Found: C, 82·4; H, 11·1. $C_{37}H_{60}O_2$ requires C, 82·8; H, 11·3%). Hydrolysis of the hexahydrobenzoate by 10% ethanolic potassium hydroxide, followed by crystallisation of the product from chloroform–methanol, gave 18α-olean-12-en-3β-ol as needles, m. p. and mixed m. p. 211—213°, $[\alpha]_D$ +48° (*c*, 0·8).

Treatment of 18α-*Olean*-12-*en*-3β-*yl Acetate with* N-*Bromosuccinimide.*—A solution of the acetate (0·5 g.) in carbon tetrachloride (50 c.c.) was refluxed with *N*-bromosuccinimide (0·4 g.) and anhydrous calcium carbonate (1 g.) for 3 hr. The filtered solution was washed with 10% sodium thiosulphate solution, and the product isolated in the usual way. Crystallisation from acetone gave oleana-9(11) : 12 : 18-trienyl acetate (300 mg.) as plates, m. p. and mixed m. p. 184—185°, $[\alpha]_D$ +525° (*c*, 0·7), $\lambda_{max.}$ 3100 Å (ε 12,000).

12-*Oxo*-18α-*oleanan*-3β-*yl Acetate.*—The following method is better than that described by Budziarek, Manson, and Spring (*loc. cit.*). A solution of 18α-olean-12-en-3β-yl acetate (7 g.) in ethyl acetate (500 c.c.) was treated at 50—60° with a solution of hydrogen peroxide (30%; 30 c.c.) in formic acid (98%; 100 c.c.) with stirring during 1 hr. The mixture was kept for 24 hr., and concentrated under reduced pressure. The crystalline solid A (m. p. 280°; 3 g.) was collected and the filtrate evaporated to dryness. The residue (4 g.) in benzene (100 c.c.) was chromatographed on a column of Grade II/III alumina (2 × 10 cm.), and the column washed with benzene (1000 c.c.) to give a crystalline solid (1 g.). This was combined with solid A and recrystallised from methanol to yield 12-oxo-18α-oleanan-3β-yl acetate (3 g.) as plates, m. p. and mixed m. p. 286—287°, $[\alpha]_D$ +77° (*c*, 1·5) (Found: C, 79·1; H, 10·8. Calc. for $C_{32}H_{52}O_3$: C, 79·3; H, 10·8%). Hydrolysis of the acetate by 5% ethanolic potassium hydroxide followed by crystallisation from methanol yielded 12-oxo-18α-oleanan-3β-ol as rods, m. p.

305—307°, $[\alpha]_D$ +89° (*c*, 0·7) which, without further purification, was treated with benzoyl chloride and pyridine to give 12-*oxo*-18α-*oleanan*-3β-*yl benzoate* which separates from chloroform–methanol as plates, m. p. 294—295°, $[\alpha]_D$ +90° (*c*, 2·5) (Found: C, 80·9; H, 9·8. $C_{37}H_{54}O_3$ requires C, 81·3; H, 9·95%). Heating this for 16 hr. with 10% ethanolic potassium hydroxide gave 12-oxo-18α-oleanan-3β-ol, m. p. and mixed m. p. 307—309°, $[\alpha]_D$ +91° (*c*, 0·7).

11β-*Bromo*-12-*oxo*-18α-*oleanan*-3β-*yl Acetate*.—The following method is better than the one described by Budziarek, Manson, and Spring (*loc. cit.*). A solution of 12-oxo-18α-oleanan-3β-yl acetate (0·8 g.) in acetic acid (100 c.c.) containing hydrobromic acid (40%; 1 c.c.) was treated at 80° with bromine (320 mg.) in glacial acetic acid (10 c.c.) during 1 hr. with stirring. The mixture was exposed to ultraviolet light (quartz flask) during the addition and for a further 4 hr. Next morning the product was isolated in the usual manner and crystallised from chloroform–methanol to give the bromo-ketone (400 mg.) as plates, m. p. 246—247°, $[\alpha]_D$ +19° (*c*, 0·7). Its infrared spectrum (in $CHCl_3$) shows a strong band at 1076 cm.$^{-1}$, in addition to bands at 1720 and 1257 cm.$^{-1}$ (acetate).

12-*Oxo*-18α-*olean*-9(11)-*en*-3β-*yl-Acetate*.—A solution of 11β-bromo-12-oxo-18α-oleanan-3β-yl acetate (250 mg.) in pyridine (30 c.c.) was refluxed for 16 hr. The pyridine was removed under reduced pressure and the product crystallised from methanol to yield 12-*oxo*-18α-*olean*-9(11)-*en*-3β-*yl acetate* as plates (125 mg.), m. p. 261—263°, $[\alpha]_D$ +145° (*c*, 0·7), $\lambda_{max.}$ 2420 Å (ε 9500) (Found: C, 79·6; H, 10·7. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%). It does not give a colour with tetranitromethane. 12-*Oxo*-18α-*olean*-9(11)-*en*-3β-*ol*, obtained from the acetate by using 5% ethanolic potassium hydroxide, crystallises from methanol as blades, m. p. 318—320°, $[\alpha]_D$ +138° (*c*, 1·3) (Found: C, 81·6; H, 10·8. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%). 12-*Oxo*-18α-*olean*-9(11)-*en*-3β-*yl benzoate* separates from chloroform–methanol as needles, m. p. 254—256°, $[\alpha]_D$ +147° (*c*, 0·7) (Found: C, 81·4; H, 9·4. $C_{37}H_{52}O_3$ requires C, 81·6; H, 9·6%).

12-Oxo-18α-olean-9(11)-en-3β-yl acetate was recovered unchanged (*a*) after 52 hours' refluxing with 15% ethanolic potassium hydroxide, followed by reacetylation, and (*b*) after 24 hours' refluxing in acetic acid with selenium dioxide.

Oxidation of 12-*Oxo*-18α-*olean*-9(11)-*en*-3β-*yl Acetate with Selenium Dioxide in Dioxan*.—A mixture of 12-oxo-18α-olean-9(11)-en-3β-yl acetate (200 mg.), dioxan (100 c.c.), and selenium dioxide (400 mg.) was kept at 200° for 18 hr. The product was isolated in the usual manner and crystallised from methanol to yield a first crop, recrystallisation of which gave 12 : 19-dioxo-18α-olean-9(11)-en-3β-yl acetate (25 mg.) as needles, m. p. and mixed m. p. 279—281°, $[\alpha]_D$ +95° (*c*, 0·5), $\lambda_{max.}$ 2420 Å (ε 10,000). Dilution of the combined mother-liquors with water gave a second crop, recrystallisation of which from aqueous methanol yielded 12 : 19-dioxo-oleana-9(11) : 13(18)-dien-3β-yl acetate (100 mg.) as plates, m. p. and mixed m. p. 240—241°, $[\alpha]_D$ −83° (*c*, 0·3), $\lambda_{max.}$ 2780 Å (ε 11,200).

12α-*Hydroxy*-18α-*olean*-9(11)-*en*-3β-*yl Acetate*.—A solution of 12-oxo-18α-olean-9(11)-en-3β-yl acetate (1 g.) in ether (500 c.c.) was refluxed with lithium aluminium hydride (1 g.) for 3 hr. The product was isolated in the usual manner (avoiding the use of mineral acid) and kept with pyridine and acetic anhydride at room temperature overnight. The acetylated product was crystallised from aqueous acetone to yield 12α-*hydroxy*-18α-*olean*-9(11)*en*-3β-*yl acetate* as needles (660 mg.), m. p. 192—193°, $[\alpha]_D$ +140° (*c*, 1·4) (Found: C, 79·0; H, 10·9. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). Light absorption: ε_{2060} 5,600. It gives a yellow colour with tetranitromethane.

18α-*Oleana*-9(11) : 12-*dien*-3β-*yl Acetate*.—A solution of 12α-hydroxy-18α-olean-9(11)-en-3β-yl acetate (400 mg.) in acetic anhydride (20 c.c.) containing freshly fused sodium acetate (400 mg.) was refluxed for 3 hr. The product was isolated in the usual manner and crystallised from aqueous acetone to yield 18α-*oleana*-9(11) : 12-*dien*-3β-*yl acetate* (150 mg.) as plates, m. p. 217—218°, $[\alpha]_D$ +255° (*c*, 1·5), $\lambda_{max.}$ 2780 Å (ε 9,400) (Found: C, 81·9; H, 10·7. $C_{32}H_{50}O_2$ requires C, 82·3; H, 10·8%). 18α-*Oleana*-9(11) : 12-*dien*-3β-*ol*, obtained from the acetate by using 5% ethanolic potassium hydroxide, separates from acetone as square plates, m. p. 203—204°, $[\alpha]_D$ +262° (*c*, 1·7) (Found: C, 84·5; H, 11·3. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%). 18α-*Oleana*-9(11) : 12-*dien*-3β-*yl benzoate* separates from chloroform–methanol as needles, m. p. 238—239°, $[\alpha]_D$ +250° (*c*, 0·5) (Found: C, 83·7; H, 9·8. $C_{37}H_{52}O_2$ requires C, 84·0; H, 9·9%). Hydrolysis for 16 hr. by 10% ethanolic potassium hydroxide gave 18α-oleana-9(11) : 12-dien-3β-ol, m. p. 200—203°, $[\alpha]_D$ +259° (*c*, 0·5).

Treatment of 18α-*Oleana*-9(11) : 12-*dien*-3β-*yl Acetate with Hydrochloric Acid*.—The 18α-dienyl acetate (100 mg.) in acetic acid (50 c.c.) and concentrated hydrochloric acid (2 c.c.) was heated on the steam-bath for 20 hr. The product was isolated in the usual manner and crystallised from chloroform–methanol to yield oleana-11 : 13(18)-dien-3β-yl acetate (50 mg.) as plates, m. p.

and mixed m. p. 224—226°, $[\alpha]_D$ −59° (*c*, 0·5), $\lambda_{max.}$ 2420, 2500, and 2600 Å (ε 23,000, 25,200, and 17,000).

18α-*Olean*-9(11)-*en*-3β-*yl Acetate*.—A solution of 12-oxo-18α-olean-9(11)-en-3β-yl acetate (125 mg.) in glacial acetic acid was shaken with hydrogen and platinum (from 100 mg. of PtO_2) for 48 hr. The product was isolated in the usual manner and crystallised from chloroform–methanol to yield **18α-*olean*-9(11)-*en*-3β-*yl acetate*** (110 mg.) as plates, m. p. 248—249°, $[\alpha]_D$ +120° (*c*, 1·2) (Found: C, 82·4; H, 11·5. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%). Light absorption: $\varepsilon_{2080} = 4550$. It gives a yellow colour with tetranitromethane. The acetate was refluxed with 5% methanolic potassium hydroxide for 3 hr. to give **18α-*olean*-9(11)-*en*-3β-*ol***. It separates from methanol as needles, m. p. 215—217°, $[\alpha]_D$ +128° (*c*, 1·1) (Found: C, 84·0; H, 12·0. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%), and gives a yellow colour with tetranitromethane.

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Triterpenoids. Part XXXVII. The Constitution of Taraxerol.*

By J. M. BEATON, F. S. SPRING, ROBERT STEVENSON, and J. L. STEWART.

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Considerations based on the reactions of taraxerol, a widely occurring triterpenoid alcohol, lead to the view that it has the structure (XVIII; R = H). This has been confirmed by the partial synthesis of taraxerol from β-amyrin (cf. *Chem. and Ind.*, 1954, 1454; 1955, 35).

IN 1923, Zellner and Röglsperger (*Sitzungsber. Akad. Wiss. Wien*, 1923, **132**, 258) isolated an alcohol, alnulin, from the bark of the grey alder (*Alnus incana* L.) (cf. Fröschl and Zellner, *ibid.*, 1930, **139**, 476) and later it was obtained from the bark of the black alder (*Alnus glutinosa* L.) (Zellner and Weiss, *ibid.*, 1925, **134**, 312). Jeger and his collaborators (Koller, Hiestand, Dietrich, and Jeger, *Helv. Chim. Acta*, 1950, **33**, 1050) demonstrated the identity of alnulin and taraxerol, isolated by Burrows and Simpson (*J.*, 1938, 2042) from the root of the dandelion (*Taraxacum officinale*) and by Dunstan, Hughes, and Smithson (*Nature*, 1947, **160**, 577; *Austral. J. Chem.*, 1953, **6**, 321) from the bark of *Litsea dealbata* (*Lauraceae*). Meanwhile, Takeda (*J. Pharm. Soc. Japan*, 1941, **61**, 117; 1942, **62**, 390; 1943, **63**, 193, 197; Takeda and Yosiki, *ibid.*, 1941, **61**, 506) isolated an alcohol, skimmiol, from *Skimmia* (*Rutaceae*) species and suggested that it was identical with taraxerol. The identity of these alcohols has been established by Brooks (*Chem. and Ind.*, 1953, 1178). We suggest that the names alnulin and skimmiol be abandoned and that, in conformity with majority practice, the alcohol from these sources should be called taraxerol.†

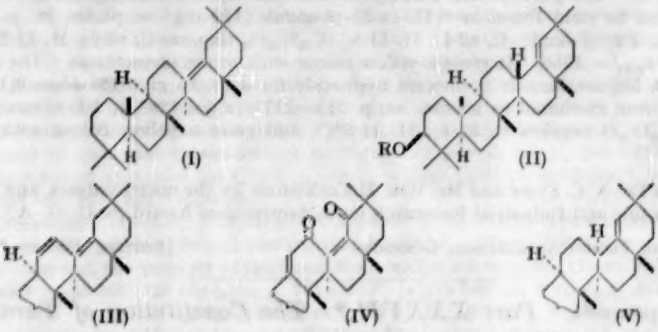
When our study of taraxerol started, a relation between this alcohol and the oleanane group of triterpenoids had been established. Takeda (*loc. cit.*) found that Clemmensen reduction of the derived ketone, taraxerone, gives olean-13(18)-ene (I) and this was confirmed by Koller *et al.* (*loc. cit.*). The excellent work of Takeda, some of which is mentioned below, led him to conclude that taraxerol is olean-18-en-3β-ol (II; R = H).‡ This opinion became untenable when germanicol, which differs from taraxerol, was shown to have this structure (Barton and Brooks, *J.*, 1951, 257). Koller *et al.* (*loc. cit.*) found that the double bond in taraxerol is of the type >C:CH· and that the hydroxyl group is present in a six-membered, or larger, ring. The Swiss workers did not construe the formation of olean-13(18)-ene from taraxerol as proof that the latter compound is an oleanane derivative.

* Part XXXVI, preceding paper.

† Tiliadin, isolated from the bark of *Tilia cordata* and *T. platyphyllos* (Bräutigam, *Arch. Pharm.*, 1900, **238**, 555; Thoms and Michaelis, *Ber. deut. pharm. Ges.*, 1916, **26**, 185; Zellner and Pelikant, *Sitzungsber. Akad. Wiss. Wien*, 1925, **134**, 616; Gerloff, *Planta*, 1936, **25**, 667), may be identical with taraxerol, but direct proof appears to be lacking.

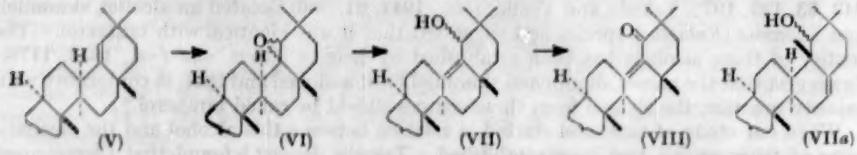
‡ In the formulæ (II)—(XXV), R = Ac unless otherwise stated.

A considerable advance in the chemistry of taraxerol was marked by a preliminary report by Brooks (*loc. cit.*) on the treatment of taraxeryl acetate with selenium dioxide. This oxidation gives oleana-11 : 13(18)-dien-3β-yl acetate (III) and 12 : 19-dioxo-oleana-9(11) : 13(18)-dien-3β-yl acetate (IV). Brooks suggested that taraxerol is 13α-germanicol



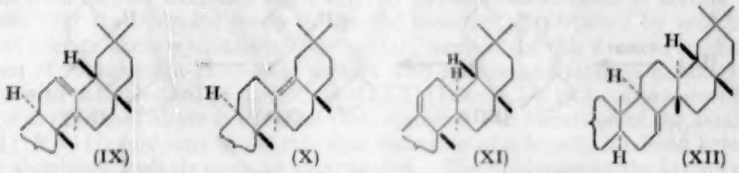
(V; R = H) with the proviso that rearrangement of the carbon skeleton does not occur during the oxidation.

For a number of reasons, we doubted the correctness of the structure (V; R = H) for taraxerol and, as our doubt transpired to be well founded, we believe they merit discussion. Takeda (*loc. cit.*) prepared taraxeryl acetate oxide, treatment of which with mineral acid yielded an unsaturated diol monoacetate, which on oxidation gave an unsaturated keto-acetate and on acetylation gave a diacetate. If taraxeryl acetate is (V), the oxide is (VI), the diol monoacetate (VII) and the keto-acetate (VIII) [19-oxo-olean-13(18)-en-3β-yl acetate]. By analogy, 19-oxo-olean-13(18)-en-3β-yl acetate (VIII) will be strongly lævorotatory as is methyl 3β-acetoxy-19-oxo-olean-13(18)-enoate ($[\alpha]_D$ −203°) and its relatives (Bilham, Kon, and Ross, *J.*, 1952, 540; Ruzicka, Grob, Egli, and Jeger, *Helv. Chim. Acta*, 1943, **26**, 1218); Takeda found that the unsaturated keto-acetate from taraxeryl acetate is dextrorotatory ($[\alpha]_D$ +4°). The reaction sequence (V) ⟶ (VII), in our view, could not represent the conversion of taraxeryl acetate into the diol monoacetate since the last compound is formulated as an allylic alcohol which is unlikely to survive the acid condition used in its preparation.



These views were not considered to be more than reasons for testing the validity of the structure (V; R = H) for taraxerol, since alternative formulæ (*e.g.*, VIIa) for the unsaturated diol monoacetate circumvent the criticisms outlined above. Two other facts, however, were difficult to reconcile with the structure (V; R = H) for taraxerol. First, dry distillation of taraxeryl benzoate gives a small yield of oleana-2 : 12-diene (Takeda, *loc. cit.*). Secondly, Clemmensen reduction of taraxerone for 24 hours gives olean-13(18)-ene, whereas similar reduction for 8 hours gives a hydrocarbon, the constants of which (m. p. 164—165°, $[\alpha]_D$ +25°) (Koller *et al.*, *loc. cit.*) correspond closely with those of a mixture of olean-12-ene and olean-13(18)-ene (Davy, Halsall, and Jones, *J.*, 1951, 458). If the hydrocarbon, m. p. 164—165°, is a mixture of the 12- and the 13(18)-ene, its conversion into pure olean-13(18)-ene by continued acid treatment is adequately explained, and, what is more important, during the Clemmensen reduction, the double bond originally present in taraxerone is moving to the 13(18)- *via* the 12 : 13-position. A simple experiment supported this view. A suspension of taraxeryl acetate in acetic acid at 90° was

treated with hydrochloric acid. The solid rapidly dissolved and after 10 minutes an excellent yield of β-amyrin acetate (olean-12-en-3β-yl acetate) (IX) was isolated. This shows that taraxerol cannot be (V; R = H), since the conversion of (V) into β-amyrin acetate (IX) would, in our view, require the conversion of the intermediate olean-13(18)-en-3β-yl acetate (X) into the thermodynamically less stable β-amyrin acetate (IX).



(IX) (X) (XI) (XII)

At this stage we concluded that, if the conversion of taraxeryl acetate into β-amyrin acetate consists in a simple double-bond movement (without molecular rearrangement), the former compound must be 13α-olean-9(11)-en-3β-yl acetate (XI), the conversion of which into β-amyrin acetate (IX) must be due to the configuration at $C_{(13)}$; it is known that the 13β-isomer of (XI), olean-9(11)-en-3β-yl acetate, is stable to mineral acid (Budziarek, Johnston, Manson, and Spring, *J.*, 1951, 3019).

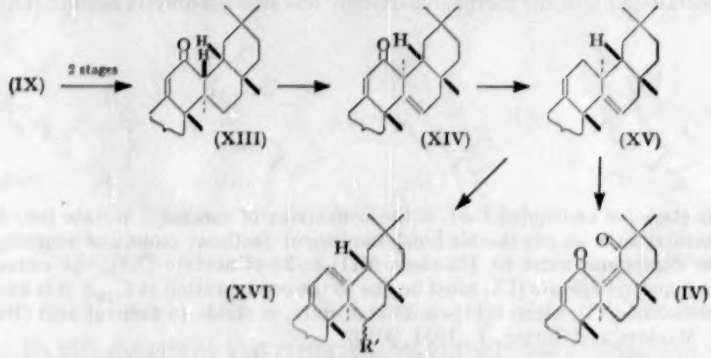
A re-examination of Takeda's oxide, unsaturated diol monoacetate, and unsaturated keto-acetate supplied a vital clue in the determination of the structure of taraxerol. The unsaturated keto-acetate does not contain an αβ-unsaturated ketone chromophore and consequently the fission of taraxeryl acetate oxide involves a molecular rearrangement. Dehydration of the diol monoacetate with phosphorus oxychloride in pyridine gives a non-conjugated dienyl acetate, catalytic hydrogenation of which yields β-amyrin acetate (IX). Hence the molecular rearrangement has *led* to an oleanane derivative and taraxerol cannot be an oleanane derivative, and more specifically, it cannot have the constitution represented by (XI; R = H).

The diol monoacetate is a hydroxy-β-amyrin acetate, the hydroxyl group in which marks the position of the double bond in taraxeryl acetate. The experiments and arguments outlined above led to consideration of the structures (XII; R = H) and (XVIII; R = H) for taraxerol. The acid-catalysed rearrangement of (XII) into β-amyrin acetate may be adequately represented as initiated by the approach of a proton to the double bond with synchronous movement of the methyl groups from $C_{(14)}$ (β) and $C_{(13)}$ (α) to $C_{(8)}$ and $C_{(14)}$ respectively, with final stabilisation by elimination of a proton from $C_{(12)}$. In its main features, this closely follows the pattern of the mechanism responsible for the conversion of euphenyl acetate into *iso*euphenyl acetate (Barton, McGhie, Pradhan, and Knight, *Chem. and Ind.*, 1954, 1325).

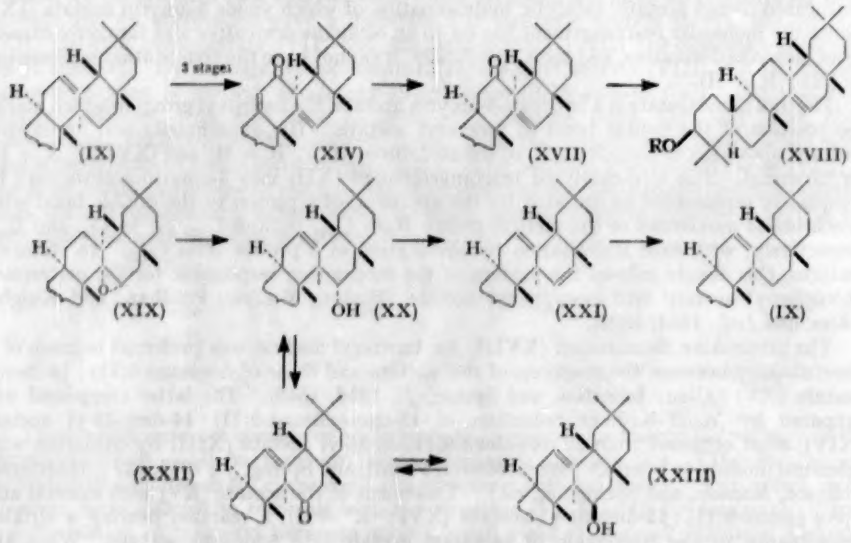
The alternative constitution (XVIII) for taraxeryl acetate was preferred because of a close analogy between the reactions of this acetate and those of *iso*olean-9(11) : 14-dienyl acetate (XV) (Allan, Johnston, and Spring, *J.*, 1954, 1546). The latter compound was prepared by Wolff–Kishner reduction of 12-oxo*iso*olean-9(11) : 14-dien-3β-yl acetate (XIV), itself obtained from 12-oxo-olean-9(11)-en-3β-yl acetate (XIII) by oxidation with selenium dioxide or bromine (Green, Mower, Picard, and Spring, *J.*, 1944, 527; Budziarek, Johnson, Manson, and Spring, *loc. cit.*). Treatment of the acetate (XV) with mineral acid gives oleana-9(11) : 12-dien-3β-yl acetate (XVI; R′ = H), a reaction bearing a striking resemblance to the conversion of taraxeryl acetate into β-amyrin acetate. When the acetate (XV) is treated with selenium dioxide, oxidation is accompanied by molecular rearrangement to give 12 : 19-dioxo-oleana-9(11) : 13(18)-dien-3β-yl acetate (IV), behaviour which again resembles that of taraxeryl acetate. Oxidation of the acetate (XV) with perbenzoic acid yields 15-hydroxyoleana-9(11) : 12-dienyl acetate (XVI; R′ = OH), presumably by rearrangement of an unstable oxide, a reaction to be compared with the conversion of taraxeryl acetate into the diol monoacetate.

A decision between the formulæ (XII) and (XVIII) for taraxeryl acetate was made in favour of the latter by partial synthesis. Reduction of 12-oxo*iso*oleana-9(11) : 14-dien-3β-yl acetate (XIV) with lithium in liquid ammonia yielded 12-oxo*iso*olean-14-en-3β-yl

acetate (XVII). By a modified (forcing) variant of the Wolff–Kishner technique (Barton, Ives, and Thomas, *J.*, 1955, 2056), the conditions for which were described to us, before their publication, by Professor D. H. R. Barton, F.R.S., to whom we express our best thanks, reduction of the ketone (XVII), followed by acetylation, yielded *iso*olean-14-en-3β-yl acetate



(XVIII) which is identical with taraxeryl acetate (taraxer-14-en-3β-yl acetate).* Since the ketone (XIV) is obtained from β-amyrin (IX), these reactions constitute a partial synthesis of taraxerol from β-amyrin. Taraxeryl acetate oxide is (XIX), the diol mono-acetate is olean-12-en-3β : 15α-diol 3-acetate (XX), the non-conjugated dienyl acetate is

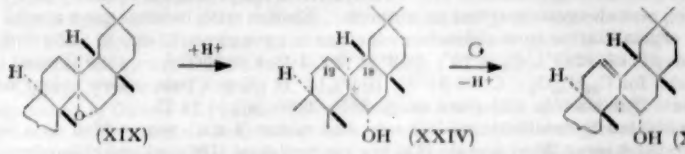


oleana-12 : 15-dien-3β-yl acetate (XXI), and the unsaturated keto-acetate is 15-oxo-olean-12-en-3β-yl acetate (XXII).

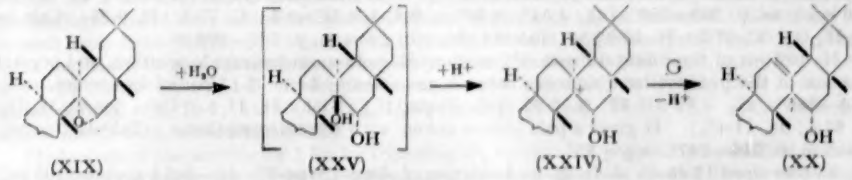
* The use of the name *iso*oleanane for the parent hydrocarbon of a naturally occurring triterpenoid is confusing because of the prior, frequent, and indiscriminate use of the prefix *iso* in the oleanane group of triterpenoids. We propose to change this name to taraxerane, and the derivatives of this hydrocarbon (in which the orientation of the hydrogen attached to $C_{(14)}$ is arbitrarily defined as α) described in the Experimental section are named accordingly. The saturated hydrocarbon obtained from dihydrotaraxerone by Clemmensen reduction (Takeda, *loc. cit.*) is almost certainly 13α-taraxerane. Taraxer-14-ene has recently been isolated from a lichen (*Cladonia deformis* Hoffm.) by Bruun (*Acta Chem. Scand.*, 1954, **8**, 1291).

The configuration of the hydroxyl group in (XX) was deduced as follows: Reduction of 15-oxo-olean-12-en-3β-yl acetate (XXII) with lithium aluminium hydride gives olean-12-ene-3β : 15β-diol (XXIII; R = H). This diol gives a monoacetate (XXIII) only and in this respect it differs from its isomer (XX; R = H) which, under the same conditions, gives a diacetate. The relation of the diol monoacetates (XX) and (XXIII) as epimers at $C_{(15)}$ was confirmed by oxidation of (XXIII) to 15-oxo-olean-12-en-3β-yl acetate (XXII). It follows that the hydroxyl group in the diol monoacetate obtained by acid fission of taraxeryl acetate oxide is equatorially bound (α); support for this decision is afforded by reduction of 15-oxo-olean-12-en-3β-yl acetate with sodium and *iso*amyl alcohol to a diol identical with that obtained by hydrolysis of (XX) (Takeda, *loc. cit.*). The isomer (XXIII) obtained as described above is the axial (15β) epimer. The formation of the axial alcohol (XXIII; R = H) conforms to the rule that reduction of a heavily hindered ketone with lithium aluminium hydride gives an axial alcohol. The hindrance to the ketone group in (XXII) is demonstrated by the fact that this compound was recovered unchanged after an attempted Wolff–Kishner reduction under normal conditions.

In our opinion the demonstration of α-configuration for the hydroxyl group in (XX) proves that the epoxide ring in taraxeryl acetate oxide likewise has the α-configuration and that the conversion of the epoxide (XIX) into (XX) is to be represented, not as a group of fully synchronous events, but rather as follows:



The degeneration of the cation (XXIV) to (XX) consists in the movement of a methyl group and the elimination of a proton from $C_{(12)}$ and these are probably synchronous. It is noteworthy that proton elimination takes place from $C_{(12)}$, and not from $C_{(18)}$, to give the thermodynamically less stable Δ^{12}-compound rather than the more stable $\Delta^{13(18)}$-isomer; the reason for this is believed to lie in the geometry of the molecule.



Fission of the oxide ring in (XIX) appears to follow the usual rule of axial opening (Barton, *J.*, 1953, 1027). This is more evident if the assumption is made that an intermediate (*trans*-)glycol (XXV) is formed; both hydroxyl groups in (XXV) are *axially* bound with respect to ring D. The change from a taraxeran-15α-ol derivative (XXV) (in which the 15-hydroxyl group is *axial*) to an oleanan-15α-ol derivative (XX) (in which the hydroxyl group is *equatorial*) and a change in the conformation of ring D are concomitant.

Experimental

Rotations were measured in $CHCl_3$ at room temperature. Absorption spectra were measured in EtOH (unless otherwise stated) with a Unicam SP.500 spectrophotometer. For chromatography, Grade II alumina and a light petroleum fraction, b. p. 60—80°, were used.

Taraxerol.—This was obtained by lithium aluminium hydride reduction of taraxerone (isolated from *Alnus glutinosa* L.); it separates as plates from chloroform–methanol and as needles from benzene, and has m. p. 282—285°, $[\alpha]_D$ ±0° (*c*, 0·6). Koller *et al.* (*loc. cit.*) give m. p. 282—283°, $[\alpha]_D$ ±0°, and Takeda (*loc. cit.*) gives m. p. 279—281°, $[\alpha]_D$ +3°. Acetylation with pyridine and acetic anhydride gave taraxeryl acetate as plates (from chloroform–methanol),

m. p. 303—305°, $[\alpha]_D$ +10·5° (*c*, 1·8). Koller *et al.* (*loc. cit.*) give m. p. 304—305°, $[\alpha]_D$ +9°, and Takeda (*loc. cit.*) gives m. p. 298—299°, $[\alpha]_D$ +13·8°. In the later stages of this work, we used taraxerol isolated from *Skimmia* by Dr. K. Takeda; we thank Dr. C. J. W. Brooks for his generosity in giving us this material.

14α : 15α-*Epoxytaraxeran*-3β-*yl Acetate*.—A solution of taraxeryl acetate (150 mg.) in chloroform (50 c.c.) was treated at 0° with a freshly prepared solution of perbenzoic acid (1·2 mol.) in chloroform, and the solution kept at 0° for 18 hr. The solution was washed with sodium hydrogen carbonate solution and water, and dried (Na_2SO_4), and the solvent removed below 15°. Crystallisation of the residue from chloroform–methanol gave 14α : 15α-epoxytaraxeran-3β-yl acetate as plates (110 mg.), m. p. 257—260°, $[\alpha]_D$ +43° (*c*, 1·0), no selective light absorption above 2000 Å. The oxide does not give a colour with tetranitromethane. Takeda (*loc. cit.*) gives m. p. 257—260°, $[\alpha]_D$ +47°.

It is essential that the per-acid solution should be freshly prepared. Thus, part of a freshly made solution of perbenzoic acid in chloroform was successfully used for the preparation of the epoxide. Use of the remaining part of the same solution after storage at 0° in the dark for 2 days gave olean-12-ene-3β : 15α-diol 3-acetate and not the epoxide. The constants (m. p. 287°, $[\alpha]_D$ +73°) given by Koller *et al.* (*loc. cit.*) for " taraxeryl acetate oxide " show that their product is olean-12-ene-3β : 15α-diol 3-acetate (see below).

Olean-12-*ene*-3β : 15α-*diol* 3-*Acetate*.—(*a*) 2N-Sulphuric acid (5 c.c.) was added to a solution of 14α : 15α-epoxytaraxeran-3β-yl acetate (80 mg.) in glacial acetic acid (100 c.c.), and the mixture heated on the steam-bath for 1 hr. A solution of the product in benzene–light petroleum (2 : 1; 25 c.c.) was chromatographed on alumina. Elution with benzene gave a solid (35 mg.), which, after crystallisation from chloroform–methanol, gave olean-12-ene-3β : 15α-diol 3-acetate as needles, m. p. 284—288°, $[\alpha]_D$ +73°, +72° (*c*, 0·9, 1·5), ε at 2060 Å = 4500 (Found : C, 79·1; H, 10·6. Calc. for $C_{32}H_{52}O_3$: C, 79·3; H, 10·8%). It gives a pale yellow colour with tetranitromethane. Takeda (*loc. cit.*) gives m. p. 283—286°, $[\alpha]_D$ +78·7°.

(*b*) Concentrated hydrochloric acid (4 c.c.) and water (4 c.c.) were added to a solution of 14α : 15α-epoxytaraxeran-3β-yl acetate (135 mg.) in methanol (100 c.c.) and chloroform (25 c.c.). The mixture was kept at room temperature for 18 hr., and the product isolated in the usual manner. Crystallisation from chloroform–methanol gave olean-12-ene-3β : 15α-diol 3-acetate as needles (80 mg.), m. p. and mixed m. p. 284—288°, $[\alpha]_D$ +74° (*c*, 1·3).

3β : 15α-*Diacetoxyolean*-12-*ene*.—Olean-12-ene-3β : 15α-diol 3-acetate (70 mg.) was treated at 100° with pyridine and acetic anhydride for 1 hr. The product, isolated in the usual way, crystallised from chloroform–methanol, to give 3β : 15α-diacetoxyolean-12-ene as needles (40 mg.), m. p. 203—205°, $[\alpha]_D$ +51°, +50° (*c*, 0·8, 1·3) (Found : C, 77·3; H, 9·85. Calc for $C_{34}H_{54}O_4$: C, 77·5; H, 10·3%). Takeda (*loc. cit.*) gives m. p. 207—208·5°.

Hydrolysis of the diacetate with 5% methanolic potassium hydroxide solution, and crystallisation of the product from aqueous acetone gave olean-12-ene-3β : 15α-diol as needles, m. p. 244—246°, $[\alpha]_D$ +82°, +83° (*c*, 0·95, 1·0) (Found : C, 81·1; H, 11·4. Calc. for $C_{30}H_{50}O_2$: C, 81·4; H, 11·4%). It gives a pale yellow colour with tetranitromethane. Takeda (*loc. cit.*) gives m. p. 246—247°, $[\alpha]_D$ +85°.

15-*Oxo-olean*-12-*en*-3β-*yl-Acetate*.—A solution of olean-12-ene-3β : 15α-diol 3-acetate (100 mg.) in benzene (10 c.c.) and acetic acid (100 c.c.) was treated at room temperature with a solution of chromium trioxide (15·3 mg.) in acetic acid (3 c.c.), added with stirring during 15 min. The mixture, after being kept overnight, was worked up in the usual way. Crystallisation of the product from chloroform–methanol gave 15-oxo-olean-12-en-3β-yl acetate as needles (70 mg.), m. p. 278—280°, $[\alpha]_D$ +27°, +27° (*c*, 1·2, 1·0), ε at 2040 Å = 4800, with no high-intensity selective absorption above 2200 Å (Found : C, 79·7; H, 10·4. Calc. for $C_{32}H_{50}O_3$: C, 79·6; H, 10·4%). It gives a pale yellow colour with tetranitromethane. Takeda (*loc. cit.*) gives m. p. 278—279°, $[\alpha]_D$ +4·1°. The ketone was recovered unchanged after being exposed to normal Wolff–Kishner reduction, followed by acetylation.

Olean-12-*ene*-3β : 15β-*diol*.—A solution of 15-oxo-olean-12-en-3β-yl acetate (207 mg.) in dry ether (130 c.c.) was refluxed for 1 hr. with lithium aluminium hydride (210 mg.), and kept overnight at room temperature. The *product*, isolated in the usual way, crystallised from aqueous acetone, to yield olean-12-ene-3β : 15β-diol (150 mg.) as needles, m. p. 194—196°, $[\alpha]_D$ +68° (*c*, 1·1, 0·9) (Found : C, 81·35; H, 11·3. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). It gives a pale yellow colour with tetranitromethane.

Olean-12-*ene*-3β : 15β-*diol* 3-*Acetate*.—(*a*) The 3β : 15β-diol (100 mg.) in pyridine and acetic anhydride was kept at room temperature overnight. The product, obtained in the usual way, crystallised from chloroform–methanol to furnish *olean*-12-*ene*-3β : 15β-*diol* 3-*acetate* (70 mg.) as

plates, m. p. 273—276°, $[\alpha]_D$ +65°, +64° (*c*, 0·9, 1·1) Found: C, 79·25; H, 11·0. $C_{32}H_{54}O_2$ requires C, 79·3; H, 10·8%).

(*b*) The diol (45 mg.) was treated with pyridine and acetic anhydride at 100° for 1 hr. Crystallisation of the product from chloroform–methanol gave the diol monoacetate as plates (20 mg.), m. p. and mixed m. p. 273—276°, $[\alpha]_D$ +64° (*c*, 0·45). A mixture of the 3β : 15β-diol 3-acetate with the isomeric 3β : 15α-diol 3-acetate (m. p. 284—288°) had m. p. 277—282°.

Chromic Acid Oxidation of Olean-12-ene-3β : 15β-diol 3-Acetate.—A solution of the 3β : 15β-diol monoacetate (75 mg.) in glacial acetic acid (60 c.c.) was treated with a solution of chromium trioxide (1·2 mol.) in acetic acid (2·7 c.c.), added dropwise with stirring during 15 min., and kept at room temperature overnight. The product, isolated in the usual way, crystallised from chloroform–methanol to give 15-oxo-olean-12-en-3β-yl acetate as needles (30 mg.), m. p. and mixed m. p. 277—279°, $[\alpha]_D$ +25° (*c*, 1·0).

Conversion of Taraxeryl Acetate into β-Amyrin Acetate.—To a suspension of taraxer-14-en-3β-yl acetate (150 mg.) in glacial acetic acid (35 c.c.) at 90°, was added concentrated hydrochloric acid (1 c.c.). After the mixture had been heated on the steam-bath for 10 min., during which the suspended solid dissolved, the solvent was rapidly removed under reduced pressure. Crystallisation of the solid from chloroform–methanol gave β-amyrin acetate as prismatic needles (80 mg.), m. p. and mixed m. p. 241—242°, $[\alpha]_D$ +82° (*c*, 0·9). Concentration of the mother-liquors gave a second crop of β-amyrin acetate (60 mg.), m. p. and mixed m. p. 238—240°.

Dehydration of Olean-12-ene-3β : 15α-diol 3-Acetate.—The diol monoacetate (100 mg.), pyridine (5 c.c.), and phosphorus oxychloride (0·5 c.c.) were heated under reflux for 2 hr. The product was isolated in the usual manner. It crystallised from methanol as needles, m. p. 153—185°. Five recrystallisations from chloroform–methanol gave *oleana-12 : 15-dien-3β-yl acetate* as needles, m. p. 207—208°, $[\alpha]_D$ +42° (*c*, 0·8), ε at 2050 Å = 8200 (Found: C, 81·8; H, 10·8. $C_{32}H_{50}O_2$ requires C, 82·3; H, 10·8%).

Hydrogenation of Oleana-12 : 15-dien-3β-yl Acetate.—A solution of the dienyl acetate (39 mg.) in glacial acetic acid (100 c.c.) was shaken in hydrogen with platinum (from 100 mg. of PtO_2) for 14 hr. Crystallisation of the product from chloroform–methanol gave β-amyrin acetate as needles (32 mg.), m. p. and mixed m. p. 238—240°, $[\alpha]_D$ +78° (*c*, 1·4).

12-Oxotaraxer-14-en-3β-yl Acetate.—A solution of 12-oxotaraxera-9(11) : 14-dien-3β-yl acetate [12-oxo*iso*oleana-9(11) : 14-dien-3β-yl acetate] (2·0 g.) in ether (75 c.c.) was added during 2 min. with stirring to a solution of lithium (600 mg.) in liquid ammonia (400 c.c.). After 3 minutes' stirring, acetone was added, and the ammonia allowed to evaporate. The product was heated for 1 hr. with acetic anhydride and pyridine, and the acetylated product purified by chromatography of its solution in light petroleum–benzene (5 : 1) on alumina. Elution of the column with light petroleum–benzene (1 : 1) yielded a solid which recrystallised from chloroform–methanol to give *12-oxotaraxer-14-en-3β-yl acetate* as needles (700 mg.), m. p. 298—300°, $[\alpha]_D$ −30°, −29° (*c*, 1·2, 1·1), absorption max. at 2060 Å (ε 4300) in EtOH, 2850 Å (ε 50) in $CHCl_3$ (Found: C, 79·9; H, 10·45. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%). It gives a pale yellow colour with tetranitromethane.

Hydrolysis of the acetate for 1 hr. by refluxing 5% methanolic potassium hydroxide solution and working up in the usual way gave *12-oxotaraxer-14-en-3β-ol* as needles (from methanol), m. p. 276—278°, $[\alpha]_D$ −45°, −43° (*c*, 1·1, 0·9) (Found: C, 80·95; H, 10·9. $C_{30}H_{48}O_2,\frac{1}{2}CH_3{\cdot}OH$ requires C, 81·0; H, 10·9%).

Reduction of 12-Oxotaraxer-14-en-3β-yl Acetate to Taraxeryl Acetate.—12-Oxotaraxer-14-en-3β-yl acetate (200 mg.) was added to a solution obtained by the addition of sodium (500 mg.) to freshly distilled diethylene glycol (25 c.c.), and the mixture heated to 180°. Anhydrous hydrazine was distilled into the mixture until the solution refluxed gently at 180°. After refluxing at this temperature for 18 hr., the mixture was distilled until the temperature rose to 210°, whereafter refluxing was continued for 24 hr. The product, isolated by means of benzene, was acetylated on the steam-bath with pyridine and acetic anhydride. Crystallisation from chloroform–methanol gave taraxer-14-en-3β-yl acetate as plates (110 mg.), m. p. 302—304°, $[\alpha]_D$ +10·5° (*c*, 1·8), undepressed in m. p. on mixing with an authentic specimen of taraxeryl acetate, m. p. 302—305°, isolated from alder bark.

Grateful acknowledgment is made of the award of Scholarships by the Colonial Products Research Council (to J. L. S.) and by the Carnegie Trust for the Universities of Scotland (to J. B.). We thank Dr. A. C. Syme and Mr. Wm. McCorkindale for the microanalyses.

THE ROYAL TECHNICAL COLLEGE, GLASGOW. [*Received, March 2nd,* 1955.]

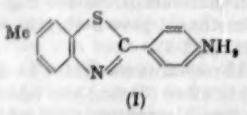
The Allegedly Isomeric Diazo-derivatives from "Dehydrothio-paratoluidine" (2-p-Aminophenyl-6-methylbenzothiazole).

By M. Aroney and R. J. W. Le Fèvre.

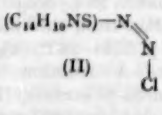
[Reprint Order No. 6118.]

Morgan and Webster's 5-methyl-1-phenylbenzothiazole-4'-*syn*- and -*anti*-diazochlorides are shown to be respectively the diazonium chloride from, and the monohydrochloride of, 2-*p*-aminophenyl-6-methylbenzothiazole. Certain sparingly soluble "diazo-derivatives" of the alleged "*syn*-chloride" should be viewed as diazonium salts with complex anions. Evidence is given that Morgan and Webster prepared an authentic diazocyanide. To date no covalent diazochloride has been isolated, although such structures may be transient intermediates in certain reactions.

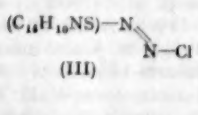
The fact that "dehydrothioparatoluidine" (2-*p*-aminophenyl-6-methylbenzothiazole) (I) could be easily diazotised by sodium nitrite in water to yield "an orange-yellow solution, which is perfectly stable at ordinary temperatures" was originally recorded without further research by Green (*J.*, 1889, **55**, 227). Morgan and Webster (*J.*, 1921, **119**, 1072), however, on repeating the process with ethyl nitrite in absolute alcohol, announced the isolation of isomeric 5-methyl-1-phenylbenzothiazole-*syn*- and -*anti*-4'-diazochlorides (II and III respectively), from which in turn the related diazocyanides and diazosulphonates could be prepared:



(I)



(II)



(III)

Whilst the existence of the last-named derivatives is quite credible (because analogies are well substantiated) that of the chlorides is less so. Two stable chloro-isomers, related as (II) to (III), would be unique in azo-chemistry, where apart from the molecule F·N=N·F (cf. Bauer, *J. Amer. Chem. Soc.*, 1947, **69**, 3104) no instance is known of halogen being covalently joined to the –N:N– unit. Moreover, there are indications that only acids weaker than hydrogen cyanide can produce isolatable diazo-compounds, stronger acids always forming diazonium salts (Saunders, "The Aromatic Diazo-compounds and Their Technical Applications," E. Arnold and Co., 2nd Edn., London, 1949, p. 388).

For these reasons a re-investigation of the materials described by Morgan and Webster seemed justifiable.

2-p-*Aminophenyl-6-methylbenzothiazole and its Diazotisation* (see Morgan and Webster, *loc. cit.*).—The crude powder, recovered from hydrochloric acid extractions of the fusion product, was distilled at atmospheric pressure (b. p. 430—440°) and crystallised from pentyl alcohol, a 31% yield of yellow needles, m. p. 193°, being obtained.

The base (5 g.) in hot ethyl alcohol (80 c.c.) was treated with excess of dry hydrogen chloride to precipitate the salt in a finely divided state. Ethyl nitrite (3 g.) or pentyl nitrite (5 g.) in alcohol was then added slowly with stirring to the mixture held between 0° and 5°. After filtration, the yellow "*syn*-diazochloride" was precipitated from the filtrate by dilution with ether. It had m. p. 139° (decomp.), in agreement with Morgan and Webster, was comparatively stable on a porous tile, and coupled readily with alkaline β-naphthol.

The yellow insoluble residue was extracted successively with boiling chloroform, cold water, and again with chloroform, the extraction with the organic solvent being repeated 14 times. The brownish-yellow amorphous powder thus obtained showed m. p. 269° (decomp.); Morgan and Webster reported 270° (decomp.) for the "*anti*-isomer."

When glacial acetic acid was substituted for alcohol and the pentyl nitrite added at room temperature, a clear solution was obtained (no residue), from which the "*syn*-chloride" could

be precipitated by ether. Similar results followed the use of alcohol as medium, and 4 equivs. of hydrochloric acid (*d* 1·16) instead of the gas; with an excess of ethyl nitrite added during 1·5 hr. a clear diazo-solution free from "*anti*-isomer" was again produced.

*The Nature of the "*syn-*Diazochloride."*—The substance was insoluble in the common non-polar solvents and dioxan, extremely soluble in water, and much less so in ethyl alcohol, glacial acetic acid, or nitrobenzene.

Comparative observations of the dependence of equivalent conductivity on concentration were made for alcoholic solutions of the "*syn*-chloride," from the amine (I), and of potassium iodide. The conductivity of the "*syn*-chloride" was of the same order as that of the iodide over the concentration range studied (10^{-3}M to 10^{-5}M) and much greater than that of the parent base. This indicated a salt-like character for the "*syn*-chloride," Hantzsch

FIG. 1. FIG. 2.

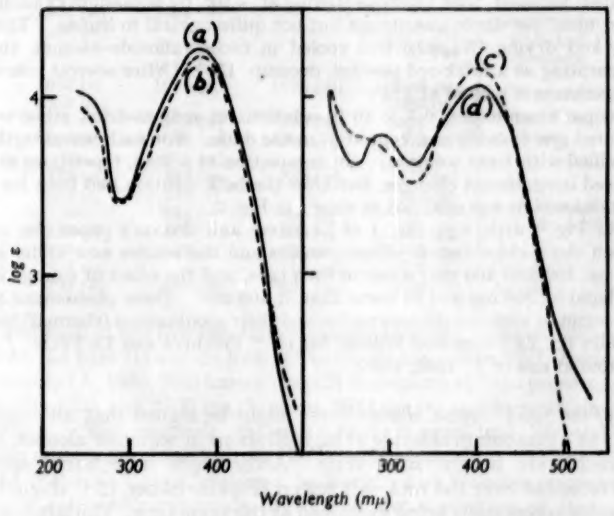


FIG. 1. *Absorption of the "*syn-*chloride" in* (*a*) *water and* (*b*) *ethanol.*

FIG. 2. *Absorption of the* syn-*cyanide,* (*c*) *freshly prepared and* (*d*) *after partial conversion into the* anti-*isomer.*

having shown that the electrolytic dissociation of diazonium salt solutions corresponds very closely to that of the analogous potassium and ammonium salts under similar conditions (cf. also Goldschmidt, *Ber.*, 1890, **23**, 3220).

The "*syn*-chloride" showed practically the same ultraviolet absorption spectrum in water and alcohol (see Fig. 1). Determinations were made with a Beckman Photoelectric Spectrophotometer, model D.U. The solute was freshly precipitated and dried immediately before the solutions were made up; coupling ability was still strong when tested against alkaline β-naphthol at the conclusion of the spectroscopic measurements. The absorption curve is simple, with a single maximum around 390 mμ of an intensity (log ε 4·2—4·3) greater than that usually found for the longer-wavelength band of genuine azo-compounds (*e.g.*, *cis*- or *trans*-azobenzenes, log ε 2·4—3·1 at 430—450 mμ; cf. Le Fèvre and Wilson, *J.*, 1949, 1106); this band apparently replaces the two bands having maxima around 300 and 400—450 mμ which are usual for the –N=N– group (Freeman, Le Fèvre, Northcott, and Worth, *J.*, 1952, 3384) and found for the diazocyanides (see below) corresponding to (II) and (III).

Wohl (*Bull. Soc. chim.*, 1939, **6**, 1319) observed that absorption curves of *ortho*- and

meta-substituted aryldiazonium chlorides display two maxima, or at least a point of inflexion, but the curves of the related *para*-derivatives have only one branch and a low maximum over the region 220—500 mμ. Since the "*syn*-chloride" is essentially a *para*-substituted aryl compound, its spectrum is therefore not inconsistent with that of a diazonium salt. The immediate relevance, however, of Fig. 1 is to Morgan and Webster's statement that the solubility of the "*syn*-chloride" in water suggests that the diazo-form undergoes a rapid tautomeric change to the diazonium condition: the spectra in water or alcohol indicate that the dissolved species is the same in each solvent; if one accepts that it is a diazonium salt in water, it must be so also in alcohol.

Diazocyanides from the "syn-Chloride."—The base (I) (5 g.) was dissolved by heat in the minimum amount of alcohol, then hydrochloric acid (10N; 15 c.c.) was added rapidly with stirring and cooling. The suspension was treated with sodium nitrite (1·5 g.) in water during 1 hr. at 5°. To the filtered diazonium chloride solution, sodium acetate (0·25 g.) and then chloroform (25 c.c.) were added, followed, with vigorous stirring at −10°, by potassium cyanide (in the least amount of water) until the whole was almost but not quite neutral to litmus. The heavy layer after separation and drying (Na_2SO_4) was cooled in carbon dioxide–alcohol, the labile *syn*-diazocyanide separating as a brick-red powder, decomp. 130°. After several hours on a porous tile at room temperature it melted at 175°.

For spectroscopic examination 0·3 × 10^{-4}M-solutions in sodium-dried ether were made up with newly prepared *syn*-cyanide and kept at 0° in the dark. For each wavelength the observation cell was refilled with fresh solution. On completion of a scan, repetitions at wavelengths used earlier showed insignificant changes, but after the bulk solution had been for 24 hr. in the dark at *ca.* 20° its spectrum was modified as shown in Fig. 2.

Comparison of Fig. 2 with, *e.g.*, Fig. 1 of Le Fèvre and Wilson's paper (*loc. cit.*) reveals a similarity between the *p*-chlorobenzenediazocyanides and the solutes now under examination: two maxima (at *ca.* 300 and 400 mμ) occur in each case, and the effect of storage is to raise the intensity of the band at 300 mμ and to lower that at 400 mμ. These phenomena are consistent with previous experience with *syn*-diazocyanides and their spontaneous (thermal) transformation into *anti*-isomerides (cf. Le Fèvre and Wilson, *loc. cit.*; Freeman and Le Fèvre, *J.*, 1950, 3128; and references cited at end of *J.*, 1949, 1595).

The Nature of the Solid "syn-Chloride."—It might be argued that although the "*syn*-chloride" reacts as a diazonium chloride at high dilutions in water or alcohol, it is possibly a covalent diazochloride in the solid state. Accordingly its infrared spectrum as a Nujol mull was recorded over the rock-salt region (Perkin–Elmer 12-C single-beam instrument), four complex compounds being examined at the same time. The latter were obtained by addition of the requisite metallic salt to an aqueous diazotisation solution [prepared from (I) with dilute hydrochloric acid and sodium nitrite], immediate precipitation occurring; these products (see Table) were stable even to drying *in vacuo* over calcium chloride.

5-Methyl-1-phenylbenzothiazole-4'-diazonium salts.

(*a*) Ferrichloride, $(R{\cdot}N_2)^+FeCl_4^-$, m. p. 113° (expln.)
(*b*) Tetrachloroiodide, $(R{\cdot}N_2)^+ICl_4^-$, m. p. 128° (expln.)
(*c*) Zincichloride, $(R{\cdot}N_2)_2^{++}ZnCl_4^{--}$, m. p. 224° (decomp.)
(*d*) Borofluoride, $(R{\cdot}N_2)^+BF_4^-$, m. p. 151° (decomp.)

From their mode of formation they were "stabilised diazonium salts" (cf. Saunders, *op. cit.*, p. 76; Hodgson and Sibbald, *J.*, 1945, 819; Chattaway, Garton, and Parkes, *J.*, 1924, 125, 1980; Schmidt and Maier, *J. prakt. Chem.*, 1932, 132, 153; Le Fèvre and Turner, *J.*, 1930, 1158). Bands are sent out in Table 1. Where it has been impossible to differentiate between closely situated absorption bands, assignments are ascribed to the group of frequencies (cf. Randall, Fowler, Fuson, and Dangl, "Infrared Determination of Organic Structures," Van Nostrand, New York, 1949; Ferguson, "Electron Structures of Organic Molecules," Prentice Hall, New York, 1952; Le Fèvre, O'Dwyer, and Werner, *Austral. J. Chem.*, 1953, 6, 341; Gilman, "Organic Chemistry," Wiley, New York, 1953, Vol. III, Chap. 2; Thompson, *J.*, 1948, 328). The term "strong"(s) indicates an absorption intensity of the order of the strongest bands throughout the given spectrum, "medium" (m)

intensities approximately one- to two-thirds of this maximum, and " weak " (w) those lower than one-third.

TABLE 1. *Infrared absorptions (cm.$^{-1}$) of the solid " syn-chloride," etc.*

" *syn*-Chloride "	Salt (*a*)	Salt (*b*)	Salt (*c*)	Salt (*d*)	Assignment
3380 (w)	—	3410 (w)	—	—	
—	3110 (w)	3090 (w)	3080 (m)	3100 (m)	C–H str.
2270 (s)	2264 (s)	2235 (s)	2275 (s)	2290 (s)	$(-N\vdots N)^+$
1576 (s)	1579 (s)	1576 (s)	1578 (s)	1582 (s)	Ph and benzothiazole-II
—	1495 (m)	—	—	1497 (m)	Ph and benzothiazole-I
—	1411 (m)	1411 (w)	—	1416 (m)	
—	—	1323 (m)	1323 (m)	—	
1312 (m)	1311 (m)	1311 (m)	1303 (m)	1312 (s)	C–N
—	—	—	1274 (m)	—	
1250 (m)	1256 (m)	1255 (m)	1252 (m)	1263 (m)	
1230 (w)	1234 (w)	—	—	1236 (w)	
1218 (w)	1220 (w)	—	—	1223 (w)	
	1205 (w)	1204 (w)	—	—	
1168 (w)	1186 (w)	—	—	1190 (w)	*para*-Disubstd. benzene and C–N and 1 : 2 : 4-trisubstd. benzene
1132 (w)	—	1132 (w)	—	1124 (m)	
—	—	1114 (w)	—	—	
1077 (m)	1083 (s)	1074 (s)	1075 (m)	1086 (s)	
1058 (w)	1059 (m)	—	—	1064 (s)	
1012 (w)	—	1006 (w)	990 (w)	1028 (s)	
966 (m)	968 (m)	971 (m)	966 (w)	972 (s)	C–N
—	—	885 (w)	—	—	
887 (w)	875 (w)	878 (w)	889 (w)	877 (w)	
845 (s)	838 (s)	846 (s)	—	843 (s)	1 : 2-Disubstd. and 1 : 2 : 4-trisubstd. benzene
—	—	834 (s)	833 (s)	—	
802 (s)	814 (s)	817 (m)	808 (s)	824 (s)	
758 (m)	759 (m)	759 (m)	764 (m)	759 (m)	
708 (w)	707 (w)	—	712 (m)	707 (w)	C–S–C
—	693 (w)	692 (w)	691 (m)	694 (m)	Ar ring

It is seen that each of the five substances absorbs strongly between 2235 and 2290 cm.$^{-1}$, a region in which the base (I) and its hydrochloride are transparent (cf. Table 3). Le Fèvre, Werner, and Aroney (*J.*, 1955, 276) have shown 21 diazonium salts to possess a common band between the limits 2231 and 2306 cm.$^{-1}$ (mean, 2261 cm.$^{-1}$) and have attributed this to the $(R–N\equiv N)^+$ cation. We conclude therefore that Morgan and Webster's " *syn*-diazochloride " is the diazonium chloride from the benzothiazole (I).

Morgan and Webster's " syn-Complexes."—Morgan and Webster prepared a number of sparingly soluble coloured compounds (by double decomposition of their alleged " *syn*-diazochloride " with soluble metallic salts containing the required anion) which they assumed to belong to the *syn*-series of diazo-structures. Three examples of these have been re-examined : the ferricyanide, the chromate, and the nitroprusside. A calcium fluoride prism of approximate resolving power 2 cm.$^{-1}$ being used, medium-strong absorptions were noted at 2275, 2264, and 2258 cm.$^{-1}$ respectively, from which we infer the presence of the diazonium group. The " *syn*-complexes " must therefore be diazonium salts with complex anions, and Morgan and Webster's " *syn*-diazo "-terminology for them must be rejected.

Other absorptions found within the range 3225—1350 cm.$^{-1}$ are included in Table 2. The

TABLE 2. *Infrared absorptions of " syn-complexes " between 3225 and 1350 cm.$^{-1}$.*

Ferricyanide	Chromate	Nitroprusside	Assignment
3090 (w)	—	3075 (w)	Aromatic C–H str.
2275 (s–m)	2264 (s–m)	2258 (s–m)	$(-N\equiv N)^+$
—	—	2131 (w)	(CN)
2107 (m)	—	—	(CN)
—	—	1895 (s)	? (NO)
1580 (s)	1579 (m)	1577 (w)	Ph and benzothiazole-I

features assigned as (CN) occur at points between those allotted as the ferrocyanide band at 2075 cm.$^{-1}$ and the ferricyanide band at 2166 cm.$^{-1}$ by Emschwiller (*Compt. rend.*, 1954, **238**, 1414) when considering the spectrum of Prussian blue. The frequency of the co-ordinated (NO) group is less certain. In $Na_2[Fe(CN)_5NO]$ it appears at 1925 cm.$^{-1}$ (Miller and Wilkins,

Analyt. Chem., 1952, **24**, 1253). The benzothiazole base absorbs weakly at 1886 cm.$^{-1}$, and it may be that (NO) absorption superposed on this produces the strong band at 1895 cm.$^{-1}$.

The Nature of the Solid "anti-Chloride."—Electrical-conductivity measurements indicated that the material was dissociated to the same extent as the hydrochloride of the benzothiazole (I). A mild red colour was still obtained with alkaline β-naphthol, even after twenty extractions with chloroform, although no increase of coupling then followed acidification (showing that the "*anti*-chloride" was not an insoluble diazoamino-derivative). Analysis further suggested that the compound was the monohydrochloride of the base (Found: C, 60·8; H, 4·6; N, 9·9. Calc. for $C_{14}H_{13}N_2SCl$: C, 60·9; H, 4·7; N, 10·1%). The m. p. was 269° (decomp.) and, when mixed with authentic hydrochloride [270° (decomp.)], was 269—270° (decomp.). The infrared spectrum of the "*anti*-isomer" showed no band at 2235—2290 cm.$^{-1}$ (and therefore seemed not to be a diazonium salt); in all other major details it resembled the monohydrochloride of (I) of which we conclude it to be a slightly impure sample.

The analytical figures published by Morgan and Webster diverge considerably from those required for the diazochloride and their accuracy is open to doubt. The fact that the "*anti*-isomer" residue is obtained only when diazotisation is carried out in alcohol and not in aqueous mineral acids or glacial acetic acid suggests that diazotisation in alcohol is much slower than in the other solvents and that unused monohydrochloride then remains as insoluble residue. This is supported by the observation that excess of ethyl nitrite and a longer reaction period results in the formation of the diazonium chloride exclusively.

TABLE 3. *Infrared absorptions of the base* (I) *and its hydrochloride.*

Base (I)	Hydrochloride	Assignments
3460 (m)	—	N–H
3298 (m)	—	N–H
3177 (m)	—	N–H
—	2490 (m)	$C-NH_3^+Cl^-$
—	2020 (w)	
1886 (w)	—	
1626 (s)	1600 (s)	Ar–NH_2; C=N
1602 (s)	1590 (s)	Ph and benzothiazole-I
1568 (m)	—	N–H
—	1495 (s)	Ph and benzothiazole-II; C–N
1305 (s)	1317 (m)	Ph and benzothiazole-II; C–N
—	1302 (m)	Ph and benzothiazole-II; C–N
1280 (m)	1277 (s)	
1256 (m)	1250 (m)	
1227 (m)	1225 (s)	
1177 (s)	1190 (m)	C–N
—	1148 (s)	
1124 (m)	1128 (m)	*p*-Disubstd. benzene
—	1120 (m)	
1060 (w)	1058 (w)	
1036 (w)	1042 (w)	
1005 (w)	1024 (w)	1 : 2 : 4-Trisubstd. benzene
—	985 (m)	
968 (s)	972 (w)	
—	953 (w)	
—	896 (m)	
887 (w)	887 (m)	C–N
864 (w)	877 (m)	
—	837 (m)	*p*-Disubstd. benzene
—	830 (m)	*p*-Disubstd. benzene
822 (s)	824 (m)	*p*-Disubstd. benzene
812 (s)	812 (s)	1 : 2 : 4-Trisubstd. benzene
—	803 (m)	1 : 2 : 4-Trisubstd. benzene
705 (w)	718 (m)	C–S–C
—	711 (w)	
693 (m)	693 (s)	Ar–ring

The Existence of Covalent Diazo-halides.—In the light of the present work it seems that stable covalent diazo-halides have not as yet been isolated. *A priori* there seems little reason for this. Many cases are known where halogen is covalently linked to nitrogen: relevantly it may be noted that geometrically isomeric ketone chloroimines are separable and have had their dipole moments measured (Theilacker and Fauser, *Annalen*, 1939, **539**, 103), that the molecule F·N≡N·F is stable and has been examined by electron diffraction (Bauer, *J. Amer. Chem. Soc.*, 1947, **69**, 3104), and that chlorine, bromine, and iodine azides exist (albeit as highly explosive substances). Throughout diazo-chemistry, however, there is much evidence for diazonium–diazo-equilibria, and the possibility has been mooted of diazo-halides' playing a transient part in certain reactions, such as coupling in the presence of pyridine (Hodgson, *J. Soc. Dyers and Colourists*, 1942, **58**, 228) or the reduction of diazonium salts by alcohols (replacement of N_2X by H; Huisgen and Nataken, *Annalen*, 1951, **573**, 181).

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Fundamental Properties of Cross-linked Poly(methacrylic Acid) Ion-exchange Resins.

By P. G. Howe and J. A. Kitchener.

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A method has been developed for preparing homogeneous, transparent gels of polymethacrylic acid cross-linked with ethylene bismethacrylate. The swelling, water-sorption, and titration curves of gels of different degrees of cross-linking have been studied in conjunction with varying degrees of neutralization with potassium hydroxide, tetraethylammonium hydroxide, barium hydroxide, and trisethylenediaminecobalt(III) hydroxide. The valency of the cation used has a particularly marked influence on the swelling, indicating a high degree of ion-association in the multivalent salts of poly(methacrylic acid).

The properties of the gels are interpreted qualitatively in terms of current theories of ion-exchange resins and chain polyelectrolytes.

The properties of ion-exchange resins depend on the nature of the functional groups, on the polymer framework, and on the degree of cross-linking. Much work has been devoted to the aromatic sulphonic acid type of resin, but comparatively little has yet been published on the aliphatic carboxylic acid type, although resins based on poly(methacrylic acid) have been commercially available for some years, and their general properties, titration curves, and kinetic behaviour have been reported in a number of papers (see, *e.g.*, Kunin and Barry, *Ind. Eng. Chem.*, 1949, **41**, 1269; Hale and Reichenberg, *Discuss. Faraday Soc.*, 1949, **7**, 79; Conway, Green, and Reichenberg, *Trans. Faraday Soc.*, 1954, **50**, 511). Marked differences are observed between the behaviour of the two classes of resin. In addition to their chemical applications, carboxylic acid resins are of particular interest for their relation to naturally occurring materials such as cellulose, alginic acid, and the proteins.

Commercial granular poly(methacrylate) resin is an unsuitable medium for careful study, first because the true degree of cross-linking is unknown (since impure divinylbenzene is used as cross-linking agent); secondly, because such resins are found to release into solution small amounts of colloidal poly(methacrylic acid) which is adsorbed on the surface of glass electrodes, giving erroneous pH values; and thirdly, because the swelling of the resins, which is of particular importance with weak-acid resins, cannot be readily determined with granular resins.

The present paper reports investigations of carefully characterised poly(methacrylic acid) resins of various degrees of cross-linking, prepared in the laboratory in the form of smooth, transparent rods.

Experimental

Preparation of Resins.—The methacrylic acid was purified by fractional distillation of the commercial product *in vacuo*.

As cross-linking agent ethylene bismethacrylate was selected as being (*a*) structurally similar to methacrylic acid, (*b*) likely to copolymerize more or less statistically with methacrylic acid (" block " co-polymers being undesirable), and (*c*) preparable in a state of purity. The stability of the ester link in the resins so prepared was remarkable: no hydrolysis could be detected after 6 months in 5M-potassium hydroxide. Ethylene bismethacrylate was prepared from methyl methacrylate (750 g.) and ethylene glycol (100 g.) by the ester-exchange method (White, *J.*, 1943, 238), 5 g. of concentrated sulphuric acid being used as catalyst and 50 g. of quinol as stabilizer. The methyl alcohol–methyl methacrylate azeotrope was distilled off through a Widmer column as formed. After removal of acid, washing, and drying, the ethylene bismethacrylate was fractionated through a Widmer column at reduced pressure, the main product being collected at 111°/8 mm. in 51% yield (Found: C, 60·3—60·4; H, 7·2—7·3. Calc. for $C_{10}H_{14}O_4$: C, 60·6; H, 7·1%).

The following procedure was developed for carrying out the polymerization so as to produce clear, homogeneous gels. Approximately equal volumes of methacrylic acid and a 0·2% aqueous solution of ammonium persulphate (as catalyst) were weighed into a small flask, together with

the requisite weighed amount of ethylene bismethacrylate (which was varied in different preparations from 0·1% to 20% of the methacrylic acid). With more than 2% of ethylene bismethacrylate, the mixture was immiscible at room temperature, but became homogeneous as the temperature was raised. The flask was therefore held in a bath of water slightly above the clearing temperature.

For the production of thin rods of resin (which proved the most convenient for handling small quantities of experimental resins) the polymerization was carried out in clean, U-shaped, thin-walled capillary tubes of 1 or 2 mm. bore, which were heated in a beaker of water, initially at 50°. The capillary tubes were charged with the previously warmed monomer mixture, and the temperature of the water-bath was then raised very slowly. The solution set to a gel at temperatures below 80°. As polymerization proceeded, the thin rod of gel was seen to contract from the sides of the tube. To complete the reaction, the water was boiled for 15 min. and then allowed to cool. The glass tubes were cut, and the resin rods gently drawn out. The rods were then boiled in water for 1 hr. to ensure that no unchanged monomer remained. Transparent rods have been obtained with as little as 0·01% and as much as 20% of cross-linking agent. The rods can be stored indefinitely in methanol, but are liable to crack when dried too rapidly, or to be attacked by moulds if left in water for a long time.

Absorption of Water by the H-*Form of Poly(methacrylic Acid) Gels.*—Resin rods of low cross-linking swell considerably in water, ethanol, and particularly methanol, and are flexible and

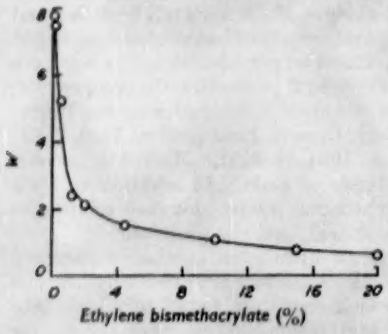


FIG. 1. *Water content (W) of hydrogen form of resin of different degrees of cross-linking (% of ethylene bismethacrylate).*

rubber-like, though weak; those with 10% of bismethacrylate are stronger and tough. No swelling is observed with acetone or ether. Individual pieces of rod can be handled with tweezers, provided special care is taken to avoid damaging those having 1% or less of cross-linking agent.

The swollen weight of the small rods was readily obtained by mopping the specimen quickly with filter-paper and weighing it in a closed bottle within 30 sec. The water content was obtained by the loss of weight when dried to constant weight in an oven at 125°. Most of the water is readily removed, but the last part is held very strongly and is not evolved at 115°. No decomposition occurs at temperatures below 140°. The reproducibility of water-content between different samples from the same batch was satisfactory and independent of the thickness and length of the rods. Results for the swelling in water of H-rods of different cross-linking are shown in Fig. 1.

If rods were dried very slowly, they could be re-swollen reversibly in water. Those of 5% or 10% cross-linking regained their original swollen weight within a few hours, and the rate of water absorption was increased by rise of temperature, but those of lower cross-linking needed several days and the process was not accelerated by heating. In fact, rise of temperature causes a contraction of the swollen gels, as with other rubber-like macromolecular materials. Maximum swelling of the weakly cross-linked gels evidently involves untangling of the chain molecules.

In studying properties such as the titration curves of the resins, the rods were not dried until after the experiment; specimens were weighed in the water-swollen condition and one sample was dried to obtain the water-content of the batch.

The sorption of water vapour by the resins from air at different relative humidities was determined approximately by suspending small pieces of rod (5—40 mg. when dry) in tubes inside bottles of controlled humidity, and weighing them until they attained constant weight.

The controlled humidities were obtained with solutions of glycerol (Johnson, *Ann. Appl. Biol.*, 1940, **27**, 295) or sodium hydroxide at 20° ± 2° (I.C.T., Vol. V). No significant hysteresis was observed. Surprisingly, the water-absorption graphs for resins of 0·15, 1, 5, and 10% cross-linking were superimposable (at least within the rather large limits of experimental error) from 0 to 90% relative humidity (Fig. 2), indicating that the considerable differences in swelling behaviour of the different resins are confined to the region 90—100% humidity. Some water-absorption data for 25° ± 0·1°, obtained by Miss N. Fraser [by using controlled humidities of the saturated salt solutions recommended by Stokes and Robinson (*Ind. Eng. Chem.*, 1949, **41**, 2013)], are shown in Fig. 3. However, no attempt has been made to examine the isotherms for different resins and different temperatures in detail, as has been done by Waxman, Sundheim, and Gregor (*J. Phys. Chem.*, 1953, **57**, 969, 974) for sulphonated polystyrene resins.

The form of the isotherms shows immediately that about 0·1 g. of water per g. of dry H-resin is very strongly absorbed; in fact, it is retained in a desiccator over solid sodium hydroxide and is removable only above 120°. This water-content corresponds to $\frac{1}{2}$ mole per mole of methacrylic acid ($C_3H_5 \cdot CO_2H$). The sorption of water is obviously by hydrogen bonding on to the carboxyl groups. Application of the Brunauer, Emmett, and Teller isotherm theory (cf. Brunauer, "The Adsorption of Gases and Vapours," O.U.P., London, 1944) leads to an estimate

FIG. 2. *Water sorption isotherm for hydrogen forms of resin at 20° (mean curve for resins of 0·1—10% of ethylene bismethacrylate).*

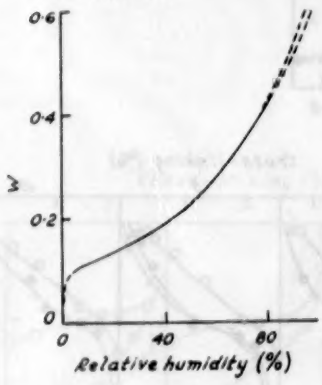
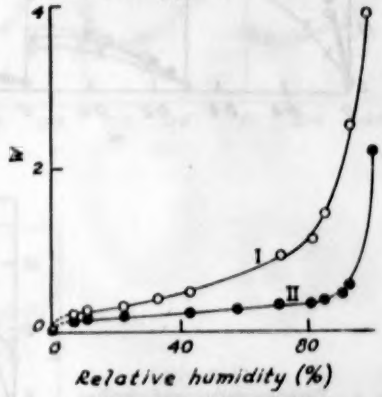


FIG. 3. *Water sorption isotherms for 1% cross-linking resin at 25° in the hydrogen form (II) and neutralized to α = 0·8 with potassium ions (I).*



of the heat of adsorption of the "first layer" of water, *viz.*, *ca.* 12 kcal. per mole of water. This indicates the formation of *two* hydrogen bonds per water molecule; thus the first water molecule is apparently bonded to two adjacent carboxyl groups.

Above 5% relative humidity the isotherm rises only slowly, and is convex to the pressure axis. Clearly, sorption is now on to low-energy sites; the hydrophilic groups have been satisfied, and the polymer chains are hydrophobic. Only at high relative humidities can the interior of the resin be rendered appreciably hydrophilic by introduction of several molecules of water around each site. It is beyond this region that swelling and stretching of the gel framework sets in.

Titration of Resin Rods with Bases.—The uptake of four typical alkalis by resins of 1, 5, and 10% cross-linking was investigated, both in the absence of neutral salt and in the presence of 0·01N- and 0·1N-solutions of the chloride of the base. On account of the slowness of the reaction and the small quantities of resin available, the titration curves were determined by equilibrating single pieces of rods, weighing 5—8 mg. when dry, with 50-ml. portions of solution in stoppered flasks, carbon dioxide being excluded by nitrogen, and the flasks being rocked gently on a tray until equilibrium was reached. The pH of the solutions was then determined on a 5-ml. sample by means of a glass electrode (with exclusion of carbon dioxide). The pH was measured again after a further 2 days' shaking to ensure that equilibrium was reached. The weights of the swollen rods, and also their diameters and lengths, were determined to obtain the degree of swelling and the approximate densities of the resin salts.

The alkalis used were potassium, tetraethylammonium, and barium hydroxides and, as an example of a soluble, strong base of a tervalent cation, trisethylenediaminecobalt(III) hydroxide,

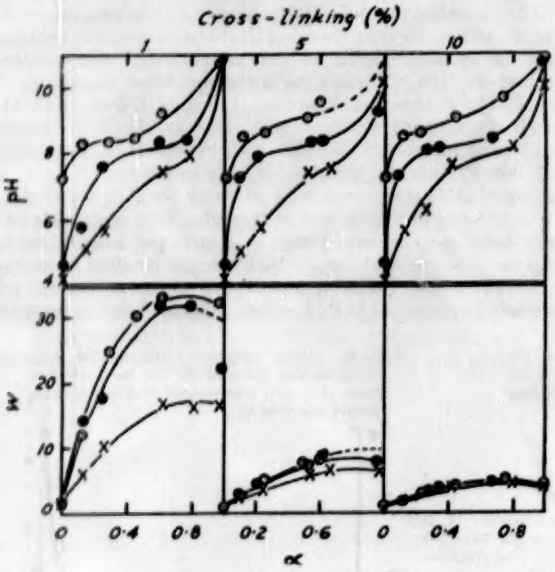


FIG. 4. *Titration curves and swelling isotherms for resins of* 1, 5, *and* 10% *cross-linking treated with potassium hydroxide, with and without added potassium chloride.*

KCl: ○, Nil; ●, 0·01N; X, 0·1N.

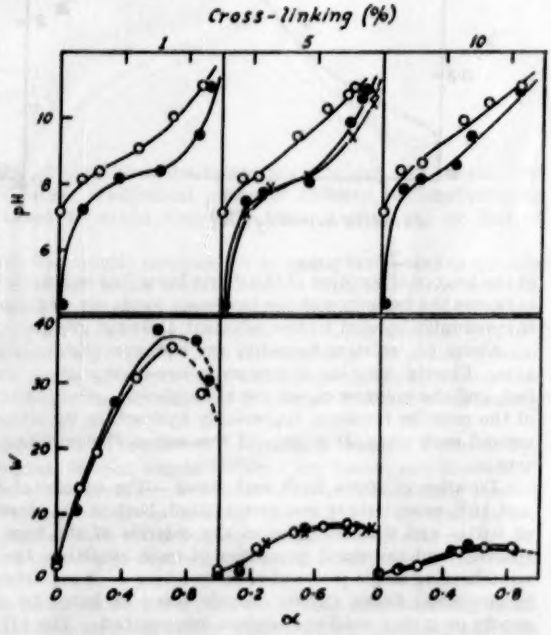


FIG. 5. *Titration curves and swelling isotherms for resins of* 1, 5, *and* 10% *cross-linking treated with tetraethylammonium hydroxide, with and without added tetraethylammonium chloride.*

$(C_2H_5)_4NCl$: ○, Nil; ●, 0·01N; X, 0·05N.

$Co(en)_3(OH)_3$, prepared from the chloride (*Inorg. Synth.*, 1946, **2**, 221) by means of a strong-base ion-exchange resin ("Deacidite FF," Permutit Co. Ltd.). The potassium and tetraethylammonium hydroxides required about 1 week to come to equilibrium with resins of 5% cross-linking, barium hydroxide needed 2 weeks, and $Co(en)_3(OH)_3$ 3 weeks. The time was shorter

with 1% cross-linked resins and longer with 10% cross-linking, the cobalt complex taking over a month for full neutralization of the latter resin.

The amount of base remaining in solution (C_{OH^-}) at equilibrium was calculated from the final pH reading by the expression, log (C_{OH^-}) = pH − 14 − log f_{OH^-}, and f_{OH^-} was estimated

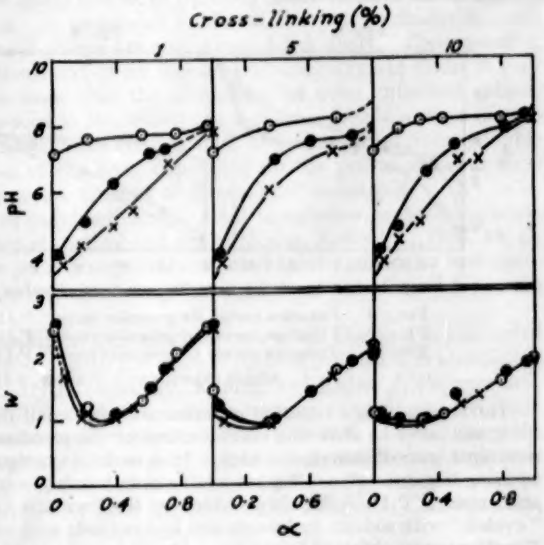


FIG. 6. *Titration curves and swelling isotherms for resins of* 1, 5, *and* 10% *cross-linking treated with barium hydroxide, with and without added barium chloride.*

$BaCl_2$: ⊙, Nil; ●, 0·01N; X, 0·1N.

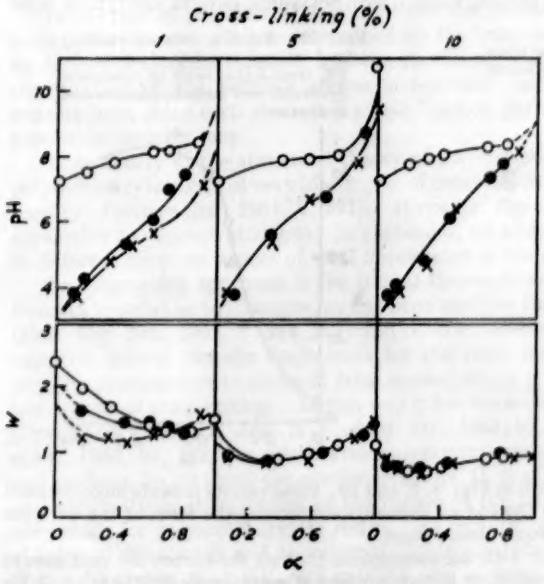


FIG. 7. *Titration curves and swelling isotherms for resins of* 1, 5, *and* 10% *cross-linking treated with trisethylenediaminecobalt*(III) *hydroxide, with and without added trisethylenediaminecobalt chloride.*

Trisethylenediaminecobalt chloride: ○, ●, 0·01N; X, 0·1N.

by use of the limiting Debye–Hückel equation. The majority of pH readings with the multivalent bases were below 8, where the difference between the added and adsorbed base was very small. The accuracy of the calculated degree of neutralization (α) is therefore not greatly affected by errors in f_{OH^-}.

Particular care was needed to obtain reliable pH values for the unbuffered solutions in the

pH region 5·5—8·5; the glass electrode, after standardization, was " conditioned " for several min. in distilled water stirred by a stream of nitrogen, and then normally gave a reading of 7·2. The water was then run off and replaced by the solution under test, and nitrogen was passed in until a steady reading was obtained. This procedure gave reproducible readings on different samples of the same solution.

FIG. 8. FIG. 9. FIG. 10.

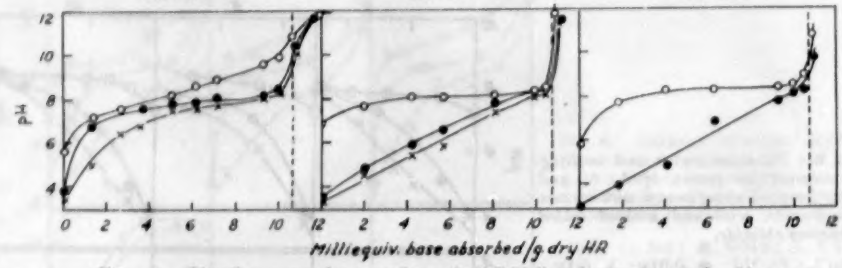


FIG. 8. *Titration curves for granular resin* " P.11 " *and potassium hydroxide.*
FIG. 9. *Titration curves for granular resin* " P.11 " *and barium hydroxide.*
FIG. 10. *Titration curves for granular resin* " P.11 " *and* $Co(en)_3(OH)_3$.
Added chloride: ○, Nil; ●, 0·01N; 0·1N.

The results of the titration experiments with small pieces of rod are summarised in Figs. 4—7, and serve to show the main features of the processes. The accuracy obtainable by this technique was, of course, not high. It is useful to compare these results with those obtained by using larger samples (0·3 g.) of a laboratory batch of a commercial, granular poly(methacrylic acid) resin (" P.11 ") (kindly provided by the Permutit Co. Ltd.). Before use, this resin was " cycled " with sodium hydroxide and hydrochloric acid solutions and then washed to pH 5—6. Titration curves obtained by the batch shaking method with potassium, barium, and trisethylene-

FIG. 11. *Settled volumes of granular resin* "P.11" *in potassium hydroxide solutions of different* pH.

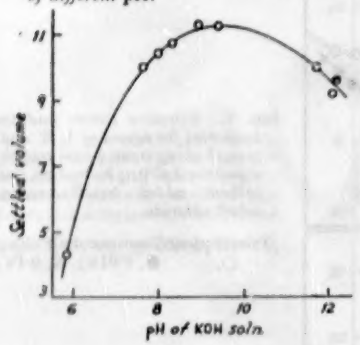
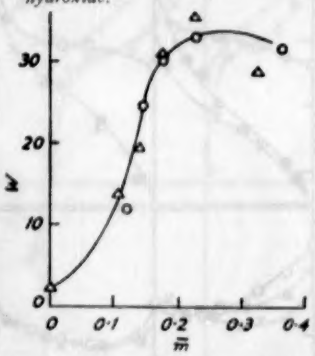


FIG. 12. *Relation between swelling and internal molality of cation, for* 1% *cross-linked resin in potassium hydroxide and tetraethylammonium hydroxide.*



diaminecobalt(III) hydroxides are shown in Figs. 8, 9, and 10; these results provide more detailed information than was available from the rod experiments concerning the form of the titration curves in the neighbourhood of the equivalence point.

The titration curves are consistent with the assumption that all the carboxylic acid groups present in the resins (as calculated from their known content of methacrylic acid) are available for salt-formation.

The swelling behaviour of the resin rods used in the titrations is also shown in Figs. 4—7; W is the weight of water taken up by 1 g. of dry H-resin.

Fig. 11 shows the settled volumes of the granular resin in potassium hydroxide solutions of different pH; the resin showed negligible volume changes in $Ba(OH)_2$ and $Co(en)_3(OH)_3$.

Discussion

Structure of the Resins.—The reversible swelling, the rubber-like elasticity of the swollen H-resins, and the fact that coherent gels are obtained with as little as 0·01% of cross-linking agent indicate that the resins consist of partially coiled chain macromolecules of a high degree of polymerization. A molecular model of the poly(methacrylic acid) chains shows clearly that the carboxyl groups are only about 4·5 Å apart. Consequently, the electrostatic field in the neighbourhood of an ionized polymethacrylate chain is very intense. Approximate calculations show that the attraction for even univalent cations is great enough to hold the counter-ions in the vicinity of a chain. Inside a three-dimensional network of chains the situation is more complicated, and an internal diffuse double layer probably exists, the extension of the layer depending on the prevailing local ionic strength, and hence being sensitive to the amount of internal diffusable salt.

Swelling.—The hydrogen-form of poly(methacrylic acid) in solution probably approximates in structure to the well-known statistical-coil model (Kuhn, *Kolloid Z.*, 1934, **68**, 2), although the solvation energy of the polar groups and the possible intramolecular hydrogen-bonding of adjacent carboxyl groups introduce complicating factors not allowed for in the theory of chain molecules.

The great expansion of the cross-linked gels which occurs when the acid is converted into its salt form is a well-known effect; with the soluble polyelectrolytes it is manifested by a great increase of intrinsic viscosity (Katchalsky, Kunzle, and Kuhn, *J. Polymer Sci.*, 1950, **5**, 283; Katchalsky, *ibid.*, 1951, **7**, 393), which arises from an extension of the chain as a result of electrostatic repulsion between the parts of the poly-ion. In this case, the counter-ions form a diffuse atmosphere in the neighbourhood of the chains, and their presence tends to screen the charges on the chains and hence reduce the extension. The screening is greatly enhanced by increase of ionic strength of the solution. Consequently, addition of salts causes a great reduction of intrinsic viscosity.

In the case of polyelectrolyte gels, where the counter-ion cloud is confined to the inter-chain interstices, swelling is determined by the balance between the osmotic effect tending to dilute the internal solution, and the elastic contractility of the network. The osmotic contribution of the polymer chains is normally negligible compared with that of the counter-ions, since each chain is a single "solute particle," but it may contribute a large number of counter ions.

The validity of the statistical theory of polyelectrolyte gels has been demonstrated for polymethacrylate gels of very low degree of cross-linking by Katchalsky, Lipson, and Eisenberg (*J. Polymer Sci.*, 1951, **7**, 571). However, the current theory is not quantitatively applicable to concentrated gels; in particular, no allowance is made for specific properties of different ions—an aspect of vital importance in ion-exchange resins.

An alternative approach is the formal thermodynamic treatment on the model of the Donnan membrane equilibrium, as has been used for the sulphonic acid resins by Glueckauf (*Proc. Roy. Soc.*, 1952, *A*, **214**, 207) and others. Water-sorption data can then be used to calculate formal osmotic coefficients for the resin materials, and the magnitude of the swelling pressure can be deduced from a comparison of the isotherms for resins of high and low degrees of cross-linking. In this way it has been clearly established (Glueckauf, *loc. cit.*; Gregor and Frederick, *Ann. N.Y. Acad. Sci.*, 1953, **57**, 87; Boyd and Soldano, *Z. Elektrochem.*, 1953, **57**, 162) for poly(styrenesulphonate) resins and for strong-base resins (Boyd and Soldano, *loc. cit.*) that the swelling pressure, Π, is a linear function of the swelling volume and substantially independent of the nature of the counter-ion. The same relation probably holds for polymethacrylate resins. At osmotic equilibrium between a resin material of internal molality $\bar{m}$ and an external, dilute solution of a 1 : 1 electrolyte of molality m, it can be shown that $\Pi V_w/RT \approx 0{\cdot}018\ (\bar{\phi}\bar{m} - 2\phi m)$, where V_w is the molar volume of water, and $\bar{\phi}$ and ϕ the osmotic coefficients in the resin and in the external solution. Application of this to resins, with K^+ or NEt_4^+ cations, in the absence of salts, gives $2\phi m \ll \bar{\phi}\bar{m}$, and $\bar{m} \propto \alpha/W$. By analogy with the findings by Boyd and others, it can be assumed that $\Pi = aW + b$, where a and b are constants for a given resin. Hence, $(aW + b) \approx 0{\cdot}018RT\bar{\phi}\bar{m}/V_w$, and W should be a linear function of $(\bar{\phi}\bar{m})$. Further, by analogy with

potassium acetate solutions, $\bar{\phi}$ might be expected to be about 0·9 and not very sensitive to concentration in the region of 1M. Such elementary considerations would therefore lead one to expect that W would be roughly linear with $\overline{m}$.

Examination of the data shows that these expectations are not even approximately realised. The W–$\overline{m}$ graph is strongly sigmoid (Fig. 12). The swelling in the region $\alpha = 0$—0·5 is more nearly proportional to $\overline{m}^2$, suggesting that increasing electrostatic repulsion between the polymer chains contributes as much to the extension as does the osmotic effect of the counter-ions. Alternatively, neutralization of the carboxyl groups may be eliminating intramolecular hydrogen bonding and thus weakening the mechanical strength of the gel. An analogous effect has been noticed in the viscosity of solutions of partially neutralized polymeric acids (Katchalsky *et al.*, *loc. cit.*). Beyond $\alpha = 0{\cdot}5$ this effect would be complete, and the declining effect of increase of $\overline{m}$ can be ascribed to the pronounced fall of $\bar{\phi}$ with α, found for poly-acid salts in solution (Kern, *Z. phys. Chem.*, 1938, *A*, **181**, 249, 283; 1939, *A*, **184**, 197, 302; Katchalsky *et al.*, *loc. cit.*). This is an electrostatic effect due to the high charge density on the polymer chains (Lipson and Katchalsky, *J. Polymer Sci.*, 1954, **13**, 43).

The marked effect of salts in de-swelling the resins of lower cross-linking is, of course, due primarily to the counter-osmotic pressure of the external solution. The swelling of the fully neutralized 1% cross-linked potassium resin is approximately halved by addition of 0·1M-potassium chloride in the external solution. This suggests that for this case (by applying the swelling energy theory and neglecting internal potassium chloride),

$$[\bar{\phi}\overline{m}]_{\text{no salt}} \approx 2[\bar{\phi}\overline{m} - 2\phi m]_{0\cdot1\text{M-salt}}$$

which leads to the conclusion that $\bar{\phi} \approx 0{\cdot}35$. This can be compared with the value of 0·17 found by Kern (*loc. cit.*) for a solution of sodium polyacrylate. Thus, even potassium ions have a low osmotic activity in the neighbourhood of the poly-ion chains.

The swelling curves for Ba^{++} and $Co(en)_3^{+++}$ (with $W < 2{\cdot}5$) are in striking contrast to those for K^+ and NEt_4^+ (with W up to 37). The actual de-swelling of 1% cross-linked resin in the hydrogen-form, when partly neutralised by Ba^{++}, must be due to contraction of the polymer chains on replacement of two carboxyl groups by $\cdot CO{\cdot}O^-{\cdot}Ba^{++}{\cdot}O^-{\cdot}OC\cdot$, the Ba^{++} ion being strongly associated with the carboxylate ions. At higher values of α, a small positive swelling is present, showing that the Ba^{++} ions are not entirely associated. The fully neutralized Ba-resin (1% cross-linked) has a " normality " of 4·6, whereas that of the corresponding K-resin is only 0·35. The osmotic coefficient of the barium resin material is roughly about 0·004.

The tervalent $Co(en)_3^{+++}$ ion produces no significant swelling. This ion must therefore be almost entirely associated with the polymethacrylate chains.

Titration Curves.—As with the swelling curves, the titration curves do not agree with those expected from the elementary theory for the neutralization of a monomeric weak acid. They are also markedly different from those obtained with materials such as wool, where the ionizing groups act as isolated sites (Gilbert and Rideal, *Proc. Roy. Soc.*, 1943, *A*, **182**, 335; Alexander and Kitchener, *Text. Res. J.*, 1950, **20**, 203). The abnormal forms are due to (*a*) electrostatic activity coefficient effects for the polymer ions and counter-ions arising from the high charge density along the polymer chains, and (*b*) changes of the swelling energy with α and with external salt concentration. The first factor has been discussed by Katchalsky, Shavit, and Eisenberg (*J. Polymer Sci.*, 1954, **13**, 69) but the overall problem is too complicated to be analysed quantitatively in the absence of information about (*b*). The following qualitative observations must therefore suffice at present.

(1) The half-neutralization point is about pH 9, largely owing to the necessity of introducing K^+ and OH^- from the solution into the gel. The ordinary pK value of the individual carboxyl groups is known to be about 4·9 (*idem*, *ibid.*), and the electrostatic effect causes a displacement of about 2 pH units only.

(2) The displacement of the titration curves to lower pH values by addition of salts is, of course, a form of common-ion effect, since a cation must be introduced into the resin as well as H^+ being abstracted.

(3) Increase of cross-linking has little effect on the titration curve for K^+, showing that the swelling energy is small in this case, but with NEt_4^+ there is a displacement to higher pH values with higher cross-linking, and the shape of the curve at large values of α also shows that with this large ion the steric resistance is important. These conclusions are similar to those reached with sulphonated polystyrene resins (cf. Kitchener, in "Ion Exchange and Its Applications," Soc. Chem. Ind., London, 1955).

(4) With Ba^{++} and $Co(en)_3^{+++}$ the half-neutralization point is at about pH 8; the displacement by 1 pH unit is due to strong adsorption of these cations on the polymer framework—an effect already detected from the swelling measurements.

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*Oxidation of Polyhalogeno-compounds. Part I. Photochemical Oxidation of Certain Fluoroalkanes.**

By W. C. FRANCIS and R. N. HASZELDINE.

[Reprint Order No. 6072.]

Photochemical vapour-phase oxidation of compounds of the type $CF_3{\cdot}[CF_2]_n{\cdot}CFYX$ (X or Y = H, F, Cl, Br, or I) is surprisingly easy. The compounds CHF_3, CF_2Cl, CF_3Br, CF_2ClBr, CF_2Br_2, and CF_3I are degraded to carbonyl fluoride, carbon dioxide, and, by attack on the reaction vessel, silicon tetrafluoride. Carbon–carbon cleavage occurs readily in the propane series, and C_3HF_7, C_3F_7Cl, C_3F_7Br, and C_3F_7I yield carbonyl fluoride; the rate of oxidation increases in the order shown. Carbon–carbon cleavage can be substantially prevented in certain cases (*a*) by carrying out the reaction in presence of water, (*b*) by introduction of chlorine or bromine as sensitisers, particularly for compounds containing a CHF_2 group, (*c*) by control of reaction pressure and oxygen concentration, and (*d*) by use where possible of a compound which contains a CFXY group, where X and Y = halogen other than fluorine. Reaction mechanisms are proposed and correlated with the factors which affect the reactions.

THIS paper marks the beginning of a series of investigations designed to enable polyhalogeno-compounds, and in particular polyfluoro-compounds, to be converted by controlled oxidation into compounds which contain a functional group such as COF, CO_2H, CHO, or >CO. Convenient and economical methods are now available for the synthesis of fluorocarbons, and of compounds of the type RH, RCl, RBr, etc. (where R is a polyfluoro-group), but in general such compounds are chemically extremely inert and cannot be used for further synthetic work. The present paper is concerned mainly with the photochemical oxidation of compounds of the type $CF_3{\cdot}[CF_2]_n{\cdot}CFXY$ (X or Y = H, F, Cl, Br, or I), the conversion of certain of these into fluoro-acids, and the mechanism of the oxidation.

Earlier studies on the oxidation of halogeno-alkanes have usually involved methane or ethane derivatives, since only a few poly-bromo-, -chloro-, or -iodo-compounds containing more than two carbon atoms are known. Harteck and Kopsch (*Z. physikal. Chem.*, **1931**, **12**, *B*, 327) showed that carbon tetrachloride reacted only slowly with oxygen atoms produced by a silent electrical discharge at low pressure, but that chloroform and methylene chloride rapidly gave carbonyl chloride. Brenschede and Schumacher (*ibid.*, **1936**, **177**, *A*, 245) found that the quantum yield for the chlorine-sensitised photochemical oxidation of methane, methyl chloride, and methylene chloride increased from 80 to 800 in the order shown, and that carbon monoxide and hydrogen chloride, with small amounts of carbonyl chloride and water, were the main products; an unidentified explosive oil which gave a positive test for a peroxide was also isolated. Chapman (*J. Amer. Chem. Soc.*, **1935**, **57**, 419) postulated that the photochemical oxidation of chloroform to give carbonyl

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chloride, chlorine, carbon dioxide, and hydrogen chloride involved a peroxide such as $CCl_3{\cdot}O{\cdot}OH$ or $\overline{CCl_2{\cdot}O{\cdot}O}$ as intermediate. Lyons and Dickinson (*ibid.*, 1935, **57**, 443) considered that the CCl_3O_2 radical was the intermediate in the photochemical oxidation of carbon tetrachloride and that it decomposed to give carbonyl chloride, oxygen, and chlorine. More recently, Schumacher and Thürauf (*Z. physikal. Chem.*, 1941, **189**, *A*, 183) showed that pentachloroethane was photochemically oxidised to trichloroacetyl chloride and carbonyl chloride. Pentachloroethane is the only polychloro-compound containing more than one carbon atom to be studied. Polybromo-compounds similarly yielded the carbonyl halide (*e.g.*, $CBr_4 \longrightarrow COBr_2 + Br_2$; Koblitz, Meissner, and Schumacher, *Ber.*, 1937, **70**, 1080). The velocity of the photochemical decomposition of alkyl iodides has long been known to be increased markedly by traces of oxygen, and peroxide intermediates have usually been postulated; these, on decomposition, are believed to give the aldehydes, alcohols, acids, etc., which are the products of such photochemical oxidations (see, *e.g.*, Olaert and Jungers, *Discuss. Faraday Soc.*, 1947, **2**, 222). Polyiodo-compounds have also been studied: methylene iodide, which yields carbon monoxide, hydrogen, iodine, iodine pentoxide, formaldehyde, formic acid, and glycol (Gregory and Style, *Trans. Faraday Soc.*, 1936, **32**, 724; Emschwiller, *Compt. rend.*, 1938, **206**, 746); and iodoform, carbon tetraiodide, and 1 : 1-di-iodoethane, which yield mainly carbon monoxide and are assumed to form initially the substances CHI_3O_2, CI_4O_2, and $CH_3{\cdot}CHI_2O_2$, respectively.

The fluorine compounds studied during the present work have been surprisingly readily oxidised, even those which are usually almost completely resistant to attack by basic or acidic reagents or conventional oxidising media. Light of wavelength >2200 Å was used, with silica reaction vessels; details of the techniques are given in the Experimental section. The results for the vapour-phase photochemical oxidation of a series of halogeno-methanes and -propanes are summarised in Tables 1 and 2, and are now considered under the various types of compound studied.

$CF_3{\cdot}[CF_2]_n{\cdot}H$, *e.g.*, CF_3H, C_3F_7H. These compounds are oxidised with difficulty, and then give only carbon dioxide and silicon tetrafluoride; the hydrogen is converted into water. An increase in the initial pressure of oxygen used decreases the rate of oxidation of fluoroform.

$CF_3{\cdot}[CF_2]_n{\cdot}Cl$, *e.g.*, CF_3Cl, C_3F_7Cl. Chlorotrifluoromethane is oxidised slowly, but more rapidly than fluoroform under comparable conditions, and yields carbon dioxide and silicon tetrafluoride. Chloroheptafluoropropane is similarly converted into carbon dioxide and silicon tetrafluoride more rapidly than is heptafluoropropane. The reaction involves complete carbon–carbon fission, and possible intermediate products such as chloropentafluoroethane or chlorotrifluoromethane are not produced. Table 2 reveals the retardation of oxidation of chloroheptafluoropropane by use of too high an initial pressure.

$CF_3{\cdot}[CF_2]_n{\cdot}Br$, *e.g.*, CF_3Br, C_3F_7Br. There is a marked difference between chloro- and bromo-trifluoromethane in ease of oxidation; the time required for the former compound is measured in days, for the latter in hours. Bromoheptafluoropropane is oxidised, with complete breakdown of the chain, at approximately the same rate as bromotrifluoromethane, so, once started, the breakdown of the fluorocarbon chain must occur rapidly. Possible intermediate products such as bromotrifluoromethane or bromopentafluoroethane cannot be detected.

$CF_3{\cdot}[CF_2]_n{\cdot}I$, *e.g.*, CF_3I, C_3F_7I. The perfluoroiodoalkanes undergo extensive decomposition in 1—2 hours. Not even traces of possible intermediates from heptafluoroiodopropane such as pentafluoroiodoethane, trifluoroiodomethane, trifluoroacetyl fluoride, or pentafluoropropionyl fluoride could be detected; carbon–carbon fission is complete and the oxidation of both fluoroiodides yields only carbonyl fluoride, etc.

In an attempt to isolate possible reaction intermediates or products which might be oxidised at a rate comparable with that of heptafluoroiodopropane itself, an excess of heptafluoroiodopropane over oxygen was used in one experiment; possible products such as $(C_3F_7)_2O_2$, $C_2F_5{\cdot}COF$, $C_3F_7{\cdot}OF$, C_6F_{14}, or C_3F_8I were not detected, and only carbonyl fluoride and the excess of heptafluoroiodopropane remained. That acyl fluorides are not unstable intermediates in the oxidation follows because pentafluoropropionyl fluoride is

decomposed only slowly under the conditions used; further, acyl fluorides are in fact isolated in substantial yield from the photochemical oxidation of other compounds (see Table 3).

Since no compounds containing trifluoromethyl or pentafluoroethyl groups are formed during the oxidation of heptafluoroiodopropane, it follows that the product from the initial reaction of a heptafluoropropyl radical with oxygen must decompose by carbon–carbon cleavage and complete disruption of the fluorocarbon chain at a much faster rate than the initiation reaction, which is thus rate-determining. As noted for other compounds, the

TABLE 1. *Photochemical oxidation of some halogenomethanes.*

Compound	Ratio O_2 : Compound	Press. (atm.)	Time of irradiation	Oxidation (%)	Products *
CF_3H	6·4	1·9	24 days	18	H_2O; no C_2F_6; no COF_2
CF_3Cl	4·8	1·9	25 days	32	No COF_2 or C_2F_6
CF_3Br	6·4	5·6	6·0 hr.	21	COF_2, Br_2; no C_2F_6
CF_2ClBr	6·8	5·8	6·5 hr.	58	COF_2, Br_2
CF_2Br_2	6·6	5·6	6·5 hr.	98	COF_2, Br_2
	6·6	5·6	4·0 hr.	88	COF_2, Br_2
CF_3I	6·4	1·9	1·3 hr.	40	COF_2, I_2; no C_2F_6
	6·5	5·8	4·0 hr.	95	COF_2, I_2

* CO_2 and SiF_4 produced in every case.

TABLE 2. *Photochemical oxidation of some halogenopropanes.*

Compound	Ratio O_2 : Compound	Press. (atm.)	Time of irradiation	Oxidation (%)	Products *
C_3F_7H	5	2·5	40 days	17	H_2O; no C_6F_{14}
C_3F_7Cl	9	5·4	25 days	26	No C_6F_{14}; no CF_3Cl, C_2F_5Cl
	9·6	1·2	45 days	100	No C_6F_{14}; no CF_3Cl, C_2F_5Cl
C_3F_7Br	6·4	5·6	18 hr.	67	Br_2; no C_6F_{14}; no CF_3Br, C_2F_5Br
C_3F_7I	5	2·5	1·5 hr.	48	COF_2, I_2; no C_6F_{14}
$C_2F_5{\cdot}CFCl_2$	4	1·5	6 hr.	2	COF_2
	4	2	28 hr.	38	$C_2F_5{\cdot}COF$, $CF_3{\cdot}COF$, Cl_2, COF_2
$C_2F_5{\cdot}CFClBr$	4	4·7	0·5 hr.	3	COF_2
$C_3F_5{\cdot}CFClBr$	4	4·7	10 hr.	40	$C_2F_5{\cdot}COF$, $CF_3{\cdot}COF$, COF_2, Br_2
$C_2F_5{\cdot}CFClI$	4	1·8	0·5 hr.	75	I_2, ICl, $C_2F_5{\cdot}COF$, $CF_3{\cdot}COF$, COF_2
$C_2F_5{\cdot}CFClI$	10	4·6	0·5 hr.	35	I_2, ICl, $C_2F_5{\cdot}COF$, $CF_3{\cdot}COF$, COF_2

* CO_2 and SiF_4 produced in every case.

rate of oxidation of trifluoroiodomethane or heptafluoroiodopropane is faster for a low than for a high initial pressure,

$CF_3{\cdot}[CF_2]_n{\cdot}CFCl_2$, *e.g.*, $C_2F_5{\cdot}CFCl_2$. This compound was photochemically oxidised much faster than chloroheptafluoropropane, *i.e.*, introduction of a second chlorine atom on the terminal carbon atom facilitates reaction. Unlike chloroheptafluoropropane and the compounds discussed above, products were obtained which resulted from other than complete carbon–carbon fission, namely, pentafluoropropionyl fluoride and a small amount of trifluoroacetyl fluoride (Table 3).

$CF_3{\cdot}[CF_2]_n{\cdot}CFClBr$, *e.g.*, CF_2ClBr, $C_2F_5{\cdot}CFClBr$. Bromochlorodifluoromethane liberates bromine on exposure to light in presence of oxygen, and is rapidly and completely oxidised to carbonyl fluoride, carbon dioxide, and silicon tetrafluoride.

1-Bromo-1-chlorohexafluoropropane was prepared by the reaction of 1-chloro-1-iodohexafluoropropane with bromine in the dark: $C_2F_5{\cdot}CFClI \xrightarrow{Br_2} C_2F_5{\cdot}CFClBr + IBr$. It is oxidised more readily than 1 : 1-dichlorohexafluoropropane, and gives a greater yield of pentafluoropropionyl and trifluoroacetyl fluorides (Table 3).

$F{\cdot}[CF_2]_n{\cdot}CFBr_2$, *e.g.*, CF_2Br_2. Apart from compounds which contain iodine, dibromodifluoromethane oxidises the most readily of the compounds studied; oxidation is complete in 6 hours (Table 1). The products are carbonyl fluoride, carbon dioxide, silicon tetrafluoride, and bromine, and by-products were not detected.

$CF_3{\cdot}[CF_2]_n{\cdot}CFClI$, *e.g.*, $C_2F_5{\cdot}CFClI$. The extensive photochemical oxidation of 1-chloro-1-iodohexafluoropropane occurring in only a few minutes strongly suggests that radical-chain reaction is involved (cf. the oxidation of C_3F_7Cl which is incomplete after 25 days). Comparatively little carbon–carbon cleavage occurs, and the main product is

pentafluoropropionyl fluoride (65% yield) together with smaller amounts of trifluoroacetyl fluoride (Table 3). The rate of oxidation is decreased by use of a relatively high initial pressure (Table 2).

The oxidation of this iodo-compound is probably the most convenient method available for the preparation of small amounts of pentafluoropropionic acid (cf. Haszeldine and Leedham, *J.*, 1953, 1548). The isolation of pentafluoropropionyl fluoride proves that 1-chloro-1-iodohexafluoropropane contains a C_2F_5 group, and thus further substantiates Haszeldine and Steele's claim (*J.*, 1953, 1592) that the reaction of trifluoroiodomethane with chlorotrifluorothylene yields exclusively (I) and not (II).

(I) $CF_3{\cdot}CF_2{\cdot}CFClI$ $\qquad\qquad$ $CF_3{\cdot}CFCl{\cdot}CF_2I$ (II)

Long-chain perfluoro-acids can thus be obtained by ascent of the homologous series:

$$CF_3{\cdot}[CF_2]_n{\cdot}I \xrightarrow{CF_2{:}CFCl} CF_3{\cdot}[CF_2]_n{\cdot}CF_2{\cdot}CFClI \xrightarrow{O_2,\ h\nu} CF_3{\cdot}[CF_2]_n{\cdot}CF_2{\cdot}CO_2H$$

The small amount (3%) of trifluoroacetyl fluoride which is produced by the photochemical oxidation of 1-chloro-1-iodohexafluoropropane is believed to arise by breakdown of the C_2F_5 group (see p. 2155), rather than by oxidation of small amounts of (II) present in (I), and this view is supported by the fact that a compound containing a trifluoromethyl group can be isolated from the oxidation of heptafluoroiodopropane, *i.e.*, by breakdown of a C_3F_7 group under suitable conditions (Table 3).

1-Chloro-1-iodohexafluoropropane is only very slightly attacked by oxygen in absence of light to give a small amount of a solid which is possibly a peroxide such as $(C_2F_5{\cdot}CFCl)_2O_2$; attempts to purify the material failed.

Prevention of Carbon–Carbon Cleavage.—The reactions summarised above and in Tables 1 and 2 show that photochemical oxidation is a powerful tool for the breakdown of a fluorocarbon chain. Of particular interest, however, are those reactions where carbon–carbon fission can be prevented, and a study has been made of some of the factors which might lead to an increased yield of acyl fluoride; *i.e.*, oxygen ratio, initial pressure, addition of water or aqueous base, addition of chlorine or bromine as sensitisers, and the effect of bromine or chlorine in presence of water.

Studies with bromochlorodifluoromethane support the conclusions reached earlier for fluoroform, chloroheptafluoropropane, trifluoroiodomethane, heptafluoroiodopropane, and 1-chloro-1-iodohexafluoropropane, namely, that the oxygen ratio and the initial pressure substantially affect the reaction rate. An increase in the ratio of oxygen to bromochlorodifluoromethane, the total initial pressure being kept constant, increases the percentage decomposition in any given time. An increase in the initial pressure, the oxygen to bromochlorodifluoromethane ratio being kept constant, decreases the rate of oxidation (see Table 4). The initial pressure and the ratio of oxygen to the compound under study do not change the reaction products, only their rate of formation, but, since the products can themselves be photolysed, control of these factors to give rapid oxidation with only slight destruction of products is clearly desirable. The intensity and wavelength of the light used similarly affect the rate of formation but not the nature of the products.

Addition of water as a reactant does not markedly affect the reaction involving 1-chloro-1-iodohexafluoropropane (see Table 3); the total yield of perfluorocarboxylic acids is the same as in absence of water, but there is an increase in the trifluoroacetic acid content. Sulphuric acid has no effect on the photochemical oxidation of heptafluoroiodopropane, but the addition of aqueous sodium hydroxide causes a distinct improvement, since low yields of fluoro-acids (10%, see Table 3) can be isolated.

The addition of bromine or chlorine as sensitiser can markedly change the speed and course of the reaction. The rate of decomposition of trifluoroiodomethane or fluoroform is markedly increased, but the products are the same as for the non-sensitised reaction; in particular, chlorotrifluoromethane is not produced. The rate of oxidation is similarly increased for the bromine- or chlorine-sensitised oxidation of heptafluoroiodopropane, and of particular interest is the isolation of pentafluoropropionyl and trifluoroacetyl fluoride in satisfactory yields (51%), thus showing that carbon–carbon fission can be prevented or stopped at an intermediate stage; bromine is more effective than chlorine in preventing

carbon–carbon fission. Bromine-sensitisation similarly enables acyl fluorides to be prepared from heptafluoropropane (Table 3). By contrast, addition of bromine has little or no effect on the rate of oxidation of chloroheptafluoropropane, and fails to prevent complete breakdown. Bromine increases the rate of oxidation of 1-chloro-1-iodohexafluoropropane, but does not increase the yield of pentafluoropropionyl fluoride, although the yield of trifluoroacetyl fluoride is markedly increased. In none of the halogen-sensitised reactions has the formation of compounds such as chloro- or bromo-trifluoromethane formed by the combination of perfluoroalkyl radicals with the sensitising halogen been observed.

Chlorine- or bromine-sensitisation in the presence of water gives still higher yields of fluorine compounds containing functional groups. This is illustrated by heptafluoroiodopropane and 1-bromo-1-chlorohexafluoropropane (Table 3). Studies on heptafluoropropane show that increase in the $Cl_2 : O_2$ ratio from 1 : 8 to 1 : 4 decreases markedly the extent of breakdown, yet increases the rate of oxidation considerably; bromine acts in similar manner (Table 3). Presence of both chlorine and water in the reaction mixture for the oxidation of 1-chloro-1-iodohexafluoropropane leads to a further improvement in the yield of the perfluoro-acids, with a combined yield of 91%.

The optimum conditions for the preparation of perfluoroacyl fluorides and thence perfluoro-acids from polyfluoroalkanes thus involve (*a*) a low initial pressure, (*b*) a high ratio of oxygen to polyfluoroalkane, (*c*) sensitisation by bromine or chlorine, (*d*) presence of water, (*e*) where possible presence of a CFZY group (Z or Y = H, Cl, Br, or I) at the point where oxidation is required.

Discussion.—Any mechanism for the vapour-phase oxidation of a fluoro-iodide $CF_3{\cdot}[CF_2]_n{\cdot}I$ must explain the following facts: (*a*) The reaction is fast and presumably involves a branching chain. (*b*) Fluorocarbons such as CF_4 or C_2F_6, and hypofluorites such as $CF_3{\cdot}OF$ are not reaction products. (*c*) A fluorocarbon chain is completely disrupted under relatively mild conditions. (*d*) Carbonyl fluoride is the main initial reaction product. (*e*) Compounds which absorb ultraviolet light readily are those most easily oxidised. (*f*) Addition of water and/or of chlorine or bromine prevents complete carbon–carbon fission. (*g*) Chlorine attached to the carbon atom of a terminal CFCl, CFBr, or CFI group prevents carbon–carbon fission almost completely. A chain reaction of the following type is therefore proposed, heptafluoroiodopropane being taken as example:

$$C_3F_7I \xrightarrow{h\nu} C_3F_7{\cdot} + I{\cdot} \quad (1)$$

$$C_3F_7{\cdot} + O_2 \longrightarrow C_3F_7{\cdot}O_2{\cdot} \quad (2)$$

$$C_3F_7{\cdot}O_2{\cdot} + C_3F_7I \longrightarrow C_3F_7{\cdot}O{\cdot}OI + C_3F_7{\cdot} \quad (3)$$

$$\downarrow O_2$$

$$C_3F_7{\cdot}O_2{\cdot} \longrightarrow \text{etc.}$$

$$C_3F_7{\cdot}O{\cdot}OI \xrightarrow{h\nu} C_3F_7{\cdot}O{\cdot} + {\cdot}OI \quad (4)$$

$$C_3F_7{\cdot}O{\cdot} \longrightarrow C_2F_5{\cdot} + COF_2 \quad (5)$$

and/or

$$C_3F_7{\cdot}O{\cdot} + C_3F_7I \longrightarrow C_3F_7{\cdot}OI + C_3F_7{\cdot} \quad (5a)$$

$$\downarrow O_2$$

$$C_3F_7{\cdot}O_2{\cdot} \longrightarrow \text{etc.}$$

$$C_3F_7{\cdot}OI \longrightarrow C_2F_5{\cdot} + COF_2 + I{\cdot} \quad (5b)$$

$$C_2F_5{\cdot} + O_2 \longrightarrow C_2F_5{\cdot}O_2{\cdot} \xrightarrow{C_3F_7I} C_2F_5{\cdot}O{\cdot} + C_3F_7{\cdot} + {\cdot}OI \quad (6)$$

$$\downarrow \qquad \downarrow O_2$$

$$CF_3{\cdot} + COF_2 \quad \text{etc.}$$

$$CF_3{\cdot} \longrightarrow CF_3{\cdot}O_2{\cdot} \longrightarrow CF_3{\cdot}O{\cdot} \xrightarrow{SiO_2} COF_2 + SiF_4$$

The following facts support this scheme. First, the rate of oxidation of a fluorine compound RX increases with its ability to absorb ultraviolet light, and when R = perfluoroalkyl this ability is in the decreasing sequence X = CFClI > $CF_2I \sim CFBr_2$ > CFClBr

$> CF_2Br > CFCl_2 > CF_2Cl > CF_2H > CF_3$ (see *J.*, **1953**, 1764, for ultraviolet spectra). This strongly suggests that the first step in the oxidation is the formation of a free radical (*e.g.*, $CF_2Br_2 \longrightarrow CF_2Br\cdot + Br\cdot$; $C_3F_7Cl \longrightarrow C_3F_7\cdot + Cl\cdot$). Thus, the larger the halogen atoms Z and Y in a compound RCFZY (R = fluorine or perfluoroalkyl; Z smaller than or equal to Y), *i.e.*, the smaller the C–Y bond dissociation energy (*J.*, **1953**, 1764), the greater the rate of oxidation. Hydrogen abstraction by oxygen can initiate reaction for heptafluoropropane (*e.g.*, $C_3HF_7 \xrightarrow{O_2\cdot} C_3F_7\cdot + HO_2\cdot \longrightarrow$ etc.).

Secondly, that the combination of a perfluoroalkyl radical with oxygen (equation 2) proceeds extremely readily may be deduced from the fact that the rapid photochemical chlorination of trifluoroiodomethane ($Cl\cdot + CF_3I \longrightarrow ICl + CF_3\cdot \xrightarrow{Cl_2} CF_3Cl + Cl\cdot$) is completely prevented by addition of oxygen, even with a chlorine : oxygen ratio as high as 3 : 1; the CF_3 radical combines exclusively with oxygen to give ultimately carbonyl fluoride. This also explains why products such as C_2F_5X or CF_3X are not formed during photochemical oxidation of C_3F_7X (X = Cl or Br).

Thirdly, the reaction scheme enables the rapid destruction of a fluorocarbon chain to be readily visualised. Direct analogies with mechanisms proposed for oxidation of hydrocarbon radicals are unsuitable, since there is probably a fundamental difference in mechanism caused by the fact that the C–F bond dissociation energy is higher than that for C–H, so that radical abstraction and disproportionation reactions to give products such as $C_2F_5\cdot OF$, C_2F_5, C_3F_8, or $C_2F_5\cdot COF$ do not occur. The fate of a C_3F_7O radical produced by the chain reaction (equations 3 and 4) will depend upon its environment. In the gas phase it will decompose according to equation 5 by loss of carbonyl fluoride and formation of a fluorocarbon radical containing one less CF_2 group; this new radical can then undergo a similar cycle of reactions to yield carbonyl fluoride and a CF_3 radical. In presence of liquid fluoroiodoalkane the alternative mode of decomposition of a $C_3F_7\cdot O$ radical [equations (*5a*) and (*5b*)] will be of particular importance.

Fourthly, decomposition of intermediates in the chain reaction in presence of water (*e.g.*, $C_3F_7\cdot OI \xrightarrow{NaOH} C_3F_7\cdot OH + NaOI \xrightarrow{-2F^-} C_2F_5\cdot CO_2H$) explains why small amounts of trifluoroacetic and pentafluoropropionic acids are formed during photochemical oxidation of heptafluoroiodopropane in presence of aqueous sodium hydroxide although the acyl fluorides are not produced under anhydrous conditions.

The photochemical oxidation of 1 : 1-dichloro-, 1-bromo-1-chloro-, and 1-chloro-1-iodohexafluoropropane gives high yields of acyl fluorides (Table 3) in sharp contrast to the oxidation of 1-bromo-, -chloro-, or -iodo-heptafluoropropane. Introduction of chlorine on to the terminal carbon atom must thus cause the change, and it is suggested that the initial reaction,

$$C_2F_5\cdot CFClX \xrightarrow{h\nu} C_2F_5\cdot CFCl\cdot \xrightarrow{O_2} C_2F_5\cdot CFCl\cdot O_2\cdot \longrightarrow C_2F_5\cdot CFCl\cdot O\cdot$$

is followed by the competing reactions,

$$(a)\ C_2F_5\cdot CFCl\cdot O\cdot \longrightarrow COFCl + C_2F_5\cdot \xrightarrow{O_2} \text{etc.}$$

and

$$(b)\ C_2F_5\cdot CFCl\cdot O\cdot \longrightarrow C_2F_5\cdot COF + Cl\cdot\ (X = Cl, Br, \text{or } I)$$

with the chlorine-atom expulsion reaction (*b*) predominating over the chain-degradation reaction (*a*) under suitable conditions.

The most interesting results of the present work are those summarised in Table 3, since they show that it is possible to prevent complete breakdown of a perfluoroalkyl radical by introducing chlorine or bromine as sensitisers. The formation of acyl fluorides in this way probably means that a radical intermediate containing bromine or chlorine is involved, *e.g.*,

$$(A)\ C_3F_7\cdot \xrightarrow{O_2} C_3F_7\cdot O_2\cdot \longrightarrow C_3F_7\cdot O\cdot \xrightarrow{Cl_2} C_3F_7\cdot OCl$$

followed by either

$$(i)\ C_2F_5\cdot CF_2\cdot OCl \longrightarrow C_2F_5\cdot COF + ClF$$

or

$$(ii)\ C_2F_5\cdot CF_2\cdot OCl \longrightarrow C_2F_5\cdot CFCl\cdot OF \xrightarrow{C_3F_7I} IF + C_2F_5\cdot CFCl\cdot O\cdot \longrightarrow C_2F_5\cdot COF + Cl\cdot$$

$$(B)\ C_3F_7\cdot \xrightarrow{O_2} C_3F_7\cdot O_2\cdot \xrightarrow{Cl_2} C_3F_7\cdot O_2Cl \longrightarrow C_2F_5\cdot COF + FOCl$$

An alternative would be

$$(C)\ C_2F_5\cdot CF_2\cdot O\cdot + Cl\cdot \longrightarrow C_2F_5\cdot COF + ClF$$

The following points have to be considered in this connection. First, for *A*(i) or *B* to be valid, the reactions must be made energetically more favourable by presence of chlorine in the molecule of the intermediate than are the analogous reactions with $C_3F_7\cdot OI$ or $C_3F_7\cdot O_2I$. Secondly, rearrangement of the $C_2F_5\cdot CF_2\cdot OCl$ is postulated in *A*(ii), since once an intermediate such as $C_2F_5\cdot CFCl\cdot O$ has been formed, with chlorine attached to the terminal carbon atom, the subsequent reactions will follow the same course as for 1-chloro-1-iodohexafluoropropane discussed earlier to give a high yield of the acyl fluoride. This mechanism also explains why bromine is more efficient than chlorine as sensitiser, since the C–Br bond in $C_2F_5\cdot CFBr\cdot O\cdot$ will cleave homolytically more readily than C–Cl in $C_2F_5\cdot CFCl\cdot O\cdot$. Thirdly, scheme *C* would imply that the carbon–fluorine bond attached to a carbon atom carrying the oxygen with its lone electron is so appreciably weakened (*e.g.*, by resonance of the type $C_2F_5{-}\overset{F}{\underset{F}{C}}{-}O\cdot \longleftrightarrow C_2F_5{-}\overset{F}{C}{=}O)$ that abstraction of fluorine by a chlorine atom becomes possible. Fourthly, the formation of trifluoroacetyl fluoride during the chlorine-sensitised photochemical oxidation of 1-chloro- or 1-bromo-1-iodohexafluoropropane or of heptafluoroiodopropane shows that chlorine is preventing complete destruction of the C_2F_5 radicals, produced by loss of carbonyl halide from the $C_2F_5\cdot CFCl\cdot O\cdot$ or $C_2F_5\cdot CF_2\cdot O\cdot$ radical, by some mechanism of type *A*, *B*, or *C*. The fact that the amount of trifluoroacetyl fluoride formed from 1-chloro-1-iodohexafluoropropane is increased further by use of bromine supports schemes *A* or *B*, since although bromine cannot influence the rate of formation of the C_2F_5 radical from $C_2F_5\cdot CFCl\cdot O$, or the yield of pentafluoropropionyl

TABLE 3. *Preparation of fluoro-acids by photochemical oxidation.*

Compound.	O_2 : Compound	Initial press. (atm.)	Other reactants	Time of irradiation	Oxidation (%)	Products (yield)
C_3F_7I	5	2	None	1·5 hr.	48	No acyl fluorides
C_3F_7I	4	5	45% aq. NaOH	24 hr.	100	$C_2F_5\cdot CO_2Na$ (5%), $CF_3\cdot CO_2Na$ (5%)
C_3F_7I	4·2	2	$Cl_2(O_2 : Cl_2 = 8{\cdot}4 : 1)$	1·5 hr.	92	$C_2F_5\cdot COF$ (24%), $CF_3\cdot COF$ (1%)
C_3F_7I	2	2	$Br_2(O_2 : Br_2 = 8{\cdot}5 : 1)$	1·5 hr.	95	$C_2F_5\cdot COF$ (38%), $CF_3\cdot COF$ (19%)
C_3F_7I	2	2	$Br_2(O_2 : Br_2 = 8{\cdot}5 : 1)$ H_2O	2 hr.	100	$C_2F_5\cdot CO_2H$ (45%), $CF_3\cdot CO_2H$ (23%)
C_3F_7H	5	3	$Br_2(O_2 : Br_2 = 8 : 1)$	30 days	58	$C_2F_5\cdot COF$ (17%), $CF_3\cdot COF$ (6%)
C_3F_7H	5	3	$Cl_2(O_2 : Cl_2 = 8{\cdot}5 : 1)$ H_2O	45 days	69	$C_2F_5\cdot CO_2H$ (12%), $CF_3\cdot CO_2H$ (<1%)
C_3F_7H	5	3	$Cl_2(O_2 : Cl_2 = 4 : 1)$ H_2O	10 days	73	$C_2F_5\cdot CO_2H$ (43%), $CF_3\cdot CO_2H$ (10%)
C_3F_7H	5	3	$Br_2(O_2 : Br_2 = 4 : 1)$ H_2O	10 days	69	$C_2F_5\cdot CO_2H$ (45%), $CF_3\cdot CO_2H$ (16%)
C_3F_7Cl	5	6	$Cl_2(O_2 : Cl_2 = 4 : 1)$ H_2O	30 days	29	No $C_2F_5\cdot CO_2H$; no $CF_3\cdot CO_2H$
C_3F_7Cl	5	6	$Br_2(O_2 : Br_2 = 4 : 1)$	30 days	25	No acyl fluorides
$C_2F_5\cdot CFCl_2$...	4	2	None	28 hr.	38	$C_2F_5\cdot COF$ (21%), $CF_3\cdot COF$ (2%)
$C_2F_5\cdot CFClBr$	5	5	None	10 hr.	40	$C_2F_5\cdot COF$ (45%), $CF_3\cdot COF$ (8%)
$C_2F_5\cdot CFClBr$	5	5	$Br_2(O_2 : Br_2 = 4 : 1)$ H_2O	10 hr.	47	$C_2F_5\cdot CO_2H$ (51%), $CF_3\cdot CO_2H$ (16%)
$C_2F_5\cdot CFClI$	4	2	None	0·5 hr.	75	$C_2F_5\cdot COF$ (65%), $CF_3\cdot COF$ (3%)
$C_2F_5\cdot CFClI$	5	2	Water	4·5 hr.	100	$C_2F_5\cdot CO_2H$ (55%), $CF_3\cdot CO_2H$ (13%)
$C_2F_5\cdot CFClI$	5	2	$Br_2(O_2 : Br_2 = 4 : 1)$	0·5 hr.	90	$C_2F_5\cdot COF$ (69%), $CF_3\cdot COF$ (21%)
$C_2F_5\cdot CFClI$	5	3	$Cl_2(O_2 : Cl_2 = 1 : 1)$ H_2O	4·5 hr.	100	$C_2F_5\cdot CO_2H$ (73%), $CF_3\cdot CO_2H$ (18%)

fluoride, it is more efficient than chlorine in preventing breakdown of a perfluoroalkyl radical such as C_2F_5 (*e.g.*, cf. C_3F_7I, Table 3).

The effect of sensitisers is well illustrated by comparison of the photolytic oxidation of 1-chloro- and 1*H*-heptafluoropropane. In absence of sensitiser the chloro-compound is photolysed only slowly, but more rapidly than is heptafluoropropane, and the rate is scarcely affected by bromine or chlorine sensitisation, since these halogens cannot facilitate the initiation step ($C_3F_7Cl \longrightarrow C_3F_7\cdot + Cl\cdot$). By contrast the photolysis of heptafluoropropane is appreciably accelerated, since hydrogen is abstracted by the sensitiser (*e.g.*, $Br\cdot + C_3F_7H \longrightarrow C_3F_7\cdot + HBr$; cf. $Cl\cdot + C_3F_7I \longrightarrow C_3F_7\cdot + ICl$), and the rate of reaction is now faster than that for chloroheptafluoropropane; furthermore, the subsequent breakdown of the C_3F_7 and C_2F_5 radicals is prevented, and acyl fluorides are formed in good yield from a compound which until now could not be converted into a compound containing a functional group.

Experimental

General Technique.—The oxidation reactions were carried out in sealed Pyrex or silica tubes of the capacity indicated. The tubes were carefully cleaned and, unless deliberately added, water, oxygen, air, mercury, iodine, etc., which might promote or inhibit free-radical reactions, were excluded. The reaction tubes were filled by condensation from a vacuum system, and were sealed whilst evacuated; the volatile reaction products were transferred to a vacuum-system for distillation and identification. Products with a b. p. too high for convenient manipulation in a vacuum-system were distilled through a short column in an apparatus designed to give minimum hold-up. Yields are based on material consumed.

All reactants were distilled before use and were spectroscopically pure; weights were obtained by measurement of the pressure change in containers of known volume or by direct weighing. Reaction products were identified by b. p., molecular weight, vapour pressure, etc., and identity was confirmed by infrared spectroscopic examination using a Perkin-Elmer Model 21 instrument. Mixtures of products which could not be separated conveniently by distillation were analysed by means of infrared spectra, sometimes after preliminary chemical separation.

Oxygen was condensed into the reaction tube from a reservoir attached to the vacuum-system by cooling the tube in liquid nitrogen. Initial pressures of oxygen up to 12 atm. were thus obtained after the tube had been sealed and allowed to reach room temperature; this pressure was considered to be the maximum for safety with the silica used (2—4-cm. diam., 1·5—2-mm. wall thickness). Usually no attempt was made to measure the amount of oxygen unchanged after reaction, and the products examined are those which are condensable by liquid oxygen. A Hanovia S-250 ultraviolet lamp was used, without the Wood's filter, at 5—15 cm. from the reaction tube. The reaction temperature was 30—40°, and the final pressure in the reaction vessel varied up to 12 atm. Pressures are calculated at 35°, and unless otherwise stated the oxidation reactions were carried out completely in the vapour phase. In experiments where the compound to be oxidised was partly in the liquid phase, the reaction vessel was shaken vigorously in a horizontal position so that both liquid and vapour were irradiated. The area of the 50-ml. silica tube which was exposed to ultraviolet light was *ca.* 50 sq. cm.; that of the 150-ml. tube was *ca.* 75 sq. cm.

Tables 1, 2, and 3 summarise the main results. Details of typical experiments follow.

Compounds of Type $CF_3\cdot[CF_2]_n\cdot H$.—(a) *Fluoroform.* The starting material, prepared from tristrifluoromethylphosphine by hydrolysis with aqueous sodium hydroxide, was spectroscopically pure (Found: *M*, 70. Calc. for CHF_3: *M*, 70). Fluoroform (0·105 g., 0·00150 mole) and oxygen (0·307 g. 0·0096 mole) in a 150-ml. silica tube (initial pressure 1·9 atm.) were irradiated for 24 days to give (*a*) water containing hydrogen fluoride and fluorosilicic acid (total *ca.* 0·00003 mole), and (*b*) carbon dioxide, silicon tetrafluoride, and fluoroform (total 0·00166 mole). Spectroscopic examination of (*b*) showed that it was mainly fluoroform and that hexafluoroethane was not a reaction product; the fraction was shaken with 20% aqueous sodium hydroxide, then redistilled to give fluoroform (0·086 g., 0·00123 mole, 82%); 18% of fluoroform had thus been oxidised.

In a second experiment, fluoroform (0·084 g., 0·0012 mole) and oxygen (0·253 g., 0·0079 mole) in a 50-ml. silica tube (initial pressure *ca.* 4·6 atm.) underwent only slight reaction (*ca.* 1%) after 31 days' irradiation. Even after allowance for the difference in the amount of radiation falling on the 50-ml. tube compared with that on the 150-ml. tube used in the first experiment

(*ca.* ⅔), it is evident that much less oxidation occurred in the second experiment. This is attributed to the effect of a higher initial pressure.

(b) 1H-*Heptafluoropropane.* Spectroscopically pure 1*H*-heptafluoropropane (0·425 g., 0·0025 mole) and oxygen (0·400 g., 0·0125 mole) in a 150-ml. silica reaction tube (initial pressure *ca.* 2·5 atm.) were irradiated for 40 days to give carbon dioxide, silicon tetrafluoride, water, and unchanged heptafluoropropane (83%).

Chlorine-sensitised Oxidation of Fluoroform.—Fluoroform (0·112 g., 0·00160 mole), oxygen (0·336 g., 0·0105 mole), and chlorine (0·0805 g., 0·001135 mole) were completely vaporised in a 150-ml. silica tube at 35° (initial pressure *ca.* 2·2 atm.). Irradiation for 13 days yielded water, hydrogen fluoride, silicon tetrafluoride, and unchanged fluoroform. Only fluoroform (0·00123 mole, 77%) remained unchanged after treatment of the gaseous products with 10% aqueous sodium hydroxide, and spectroscopic examination showed it to be uncontaminated by chlorotrifluoromethane; 23% of the fluoroform had thus been oxidised.

Halogen-sensitised Oxidation of 1H-*Heptafluoropropane.*—Heptafluoropropane (0·425 g., 0·0025 mole), oxygen (0·400 g., 0·0125 mole), water (3 ml.), and chlorine (0·1 g.) were sealed in a 150-ml. silica tube (initial pressure *ca.* 3 atm.) which was shaken vigorously in a horizontal position and exposed to ultraviolet light (45 days). The volatile products were washed with aqueous sodium hydroxide to remove the excess of chlorine and distilled *in vacuo* to give only heptafluoropropane (31%). The aqueous solution was treated with silver carbonate until neutral, and the filtered solution was evaporated to dryness to give a white solid. This was dried (P_2O_5) *in vacuo*, then extracted with ether. Evaporation of the ethereal solution to dryness gave silver pentafluoropropionate (12%) mixed with silver trifluoroacetate (<1%).

The same reaction tube, experimental techniques, and weights of heptafluoropropane and oxygen were used to investigate chlorine sensitisation with a higher chlorine concentration, and bromine sensitisation with and without the addition of water (3 ml.). The molar ratios of oxygen to halogen and the results of the experiments are summarised in Table 3.

Compounds of Type $CF_3{\cdot}[CF_2]_n{\cdot}Cl$.—(a) *Chlorotrifluoromethane.* Spectroscopically pure chlorotrifluoromethane (0·209 g., 0·002 mole) and oxygen (0·307 g., 0·0096 mole) in a 150-ml. silica tube (initial pressure *ca.* 1·9 atm.), irradiated for 25 days, gave volatile products (0·0020 mole) (Found: *M*, 95), shown by spectroscopic examination to contain chlorotrifluoromethane, silicon tetrafluoride, carbon dioxide, and a small amount (*ca.* 0·00006 mole) of an unidentified, less volatile material. After being shaken with 20% aqueous sodium hydroxide, the products were redistilled to give unchanged chlorotrifluoromethane (0·142 g., 0·00136 mole, 68%) (Found: *M*, 105. Calc. for $CClF_3$: *M*, 104·5).

(b) 1-*Chloroheptafluoropropane.* Spectroscopically pure chloro-compound (0·1329 g., 0·00065 mole) and oxygen (0·2000 g., 0·00625 mole) in a 150-ml. silica tube (initial pressure *ca.* 1·2 atm.), exposed to ultraviolet light for 45 days, yielded no unchanged compound, and the products were completely absorbed by aqueous base.

In a second experiment chloroheptafluoropropane (0·2188 g., 0·00107 mole) and oxygen (0·3072 g., 0·0096 mole) were completely in the vapour phase when sealed in a 50-ml. silica tube (initial pressure *ca.* 5·4 atm.), and irradiation for 25 days gave unchanged chloro-compound (0·1615 g., 0·00079 mole, 74%), a small unidentified fraction (0·00004 mole), and a fraction (0·00098 mole) comprising silicon tetrafluoride and carbon dioxide which was completely destroyed by aqueous sodium hydroxide. Increase in the oxygen pressure has thus considerably reduced the rate of oxidation.

Experiments carried out with chloroheptafluoropropane (0·736 g., 0·0036 mole) and oxygen (0·960 g., 0·030 mole) in a 150-ml. silica tube in presence of bromine or of chlorine and water are summarised in Table 3. Infrared spectroscopy was used to examine the products.

Compounds of Type $CF_3{\cdot}[CF_2]_n{\cdot}Br$.—(a) *Bromotrifluoromethane.* The sample used was spectroscopically pure. Bromotrifluoromethane (0·2235 g., 0·00150 mole) and oxygen (0·3072 g., 0·0096 mole), sealed in a 50-ml. silica tube (initial pressure *ca.* 5·6 atm.) and completely in the vapour phase, were exposed to ultraviolet light. An immediate reaction was apparent and bromine was liberated. After 6 hr. the condensable products (0·00170 mole) were examined spectroscopically and found to contain bromotrifluoromethane, carbonyl fluoride, silicon tetrafluoride, and carbon dioxide. Hexafluoroethane was not a product. A small unidentified, less volatile fraction (0·00004 mole) was also separated. After being shaken with 20% aqueous sodium hydroxide the products yielded only bromotrifluoromethane (0·1758 g., 0·00118 mole, 79%) (Found: *M*, 150. Calc. for $CBrF_3$: *M*, 149). Bromotrifluoromethane is not decomposed by treatment with 20% aqueous sodium hydroxide.

(b) 1-*Bromoheptafluoropropane.* Bromoheptafluoropropane was prepared in 73% yield

by irradiation of heptafluoroiodopropane (1·55 g.) and bromine (2 g.) in a sealed 150-ml. silica tube for 4·5 days. Spectroscopically pure bromoheptafluoropropane (0·374 g., 0·0015 mole) and oxygen (0·3072 g., 0·0096 mole) when sealed in a 50-ml. silica tube were completely in the vapour phase at 35° (initial pressure *ca.* 5·6 atm.). After irradiation for 18 hr. the mixture contained free bromine, unchanged bromoheptafluoropropane (0·125 g., 0·00050 mole, 33%) (Found: *M*, 253. Calc. for C_3BrF_7: *M*, 249), and a more volatile fraction (0·0056 mole) shown by spectroscopic investigation to consist mainly of carbon dioxide and silicon tetrafluoride. The last fraction was almost completely decomposed when shaken with 20% aqueous sodium hydroxide, and bromotrifluoromethane or bromopentafluoroethane is thus not a product. Bromoheptafluoropropane is stable to aqueous sodium hydroxide.

Compounds of Type $CF_3{\cdot}[CF_2]_n{\cdot}I$.—(a) *Trifluoroiodomethane.* This was prepared from silver trifluoroacetate and iodine (*J.*, 1951, 584). The iodo-compound (0·2939 g., 0·0015 mole) and oxygen (0·3072 g., 0·0096 mole), sealed in a 150-ml. silica tube (initial pressure *ca.* 1·9 atm.) and irradiated, gave a marked liberation of iodine after 15 min.; after 80 min., distillation gave unchanged trifluoroiodomethane (0·1764 g., 0·0009 mole, 60%), carbonyl fluoride, silicon tetrafluoride, and a small amount of carbon dioxide. The weight of unchanged trifluoroiodomethane was obtained after spectroscopic examination and reaction with aqueous sodium hydroxide.

In a second experiment, trifluoroiodomethane (0·894 g., 0·00456 mole) and oxygen (0·96 g., 0·030 mole), sealed in a 150-ml. silica tube (initial pressure 5·8 atm.) and irradiated for 4 hr., yielded trifluoroiodomethane (5%) isolated after treatment of its mixture with carbonyl fluoride, carbon dioxide, and silicon tetrafluoride with aqueous base.

(b) *Heptafluoro-1-iodopropane.* The reaction of silver heptafluorobutyrate and iodine yielded spectroscopically pure heptafluoroiodopropane (*J.*, 1951, 584; 1952, 4259).

(i) The iodo-compound (0·5802 g., 0·00196 mole) and oxygen (0·3072 g., 0·0096 mole) in a 150-ml. silica tube (initial pressure *ca.* 2 atm.) liberated iodine after 15 minutes' irradiation with shaking (liquid phase present initially), and, after 90 min., distillation *in vacuo* gave unchanged heptafluoroiodopropane (0·3048 g., 0·00103 mole, 52%) and a mixture (0·0049 mole) of carbonyl fluoride, silicon tetrafluoride, and carbon dioxide. The products were identified spectroscopically.

(ii) In this experiment a deficiency of oxygen was used. Heptafluoroiodopropane (2·00 g., 0·0068 mole) and oxygen (0·045 g., 0·0014 mole) in a 150-ml. silica tube (initial pressure *ca.* 1·2 atm.) yielded solid iodine after 1 hour's irradiation (reaction tube shaken) and 30% of the oxygen was recovered. Fractionation and spectroscopic examination of the reaction products revealed (*a*) unchanged heptafluoroiodopropane, (*b*) a small amount of material which could not be identified by spectroscopic examination but did not contain an acyl fluoride, and (*c*) carbonyl fluoride (0·0019 mole). The carbonyl fluoride is equivalent to 67% of the oxygen taken in the initial reaction mixture, and this is in good agreement with the measured oxygen recovery (30%).

(iii) Heptafluoroiodopropane (1·64 g., 0·0055 mole), oxygen (0·5280 g., 0·0165 mole), and 50% aqueous sulphuric acid (10 ml.) in a 110-ml. silica tube (initial pressure *ca.* 4 atm.) were shaken and exposed to ultraviolet light for 36 hr. The contents of four such tubes were combined, and the aqueous solution was filtered to remove solid iodine, saturated with sodium chloride, and extracted with ether (10 × 20 ml.). After drying (Na_2SO_4), distillation gave ether and a residue (0·32 g.) which did not possess the characteristic odour of perfluorocarboxylic acids; distillation of the residue failed to give a clear-cut fraction. Heptafluoroiodopropane was completely oxidised under the conditions used, and spectroscopic examination of the volatile reaction products revealed the presence of only carbon dioxide and silicon tetrafluoride.

(iv) Heptafluoroiodopropane (4·00 g., 0·0135 mole) and oxygen (1·728 g., 0·054 mole) were sealed with an excess of sodium hydroxide (9·0 g., 0·23 mole) and water (20 ml.) in a 170-ml. silica tube (initial pressure *ca.* 9 atm.), which was shaken (liquid phase present) and irradiated for 24 hr. The contents of the tube were combined with those of a second tube (295 ml.) in which had been sealed heptafluoroiodopropane (4·00 g., 0·0135 mole), oxygen (1·728 g., 0·054 mole), sodium hydroxide (9·0 g., 0·23 mole), and water (20 ml.) (initial pressure *ca.* 5 atm.) before exposure to ultraviolet light for 48 hr. No unchanged heptafluoroiodopropane was detected. The aqueous solution was strongly acidified with 50% sulphuric acid, filtered to remove iodine, and extracted with ether (10 × 20 ml.). The dried (Na_2SO_4) ethereal solution was shaken with mercury to remove iodine, evaporated to small bulk, and neutralised with 10% aqueous sodium carbonate. Evaporation to dryness gave a solid which was extracted with anhydrous ethanol to give a mixture of sodium salts of perfluoro-carboxylic acids (0·44 g.).

The thoroughly dried mixture, analysed by means of infrared spectroscopy, authentic samples of sodium trifluoroacetate and sodium pentafluoropropionate being used to give the reference data, contained sodium pentafluoropropionate (60%) and sodium trifluoroacetate (40%). The yields of sodium pentafluoropropionate (0·00142 mole) and sodium trifluoroacetate (0·00130 mole) based on heptafluoroiodopropane are 5·3 and 4·8%.

Chlorine-sensitised Oxidation of Trifluoroiodomethane.—Trifluoroiodomethane (0·298 g., 0·00152 mole), chlorine (0·531 g., 0·00748 mole), and oxygen (0·081 g., 0·00252 mole), sealed in a 50-ml. silica tube (initial pressure 5·8 atm.), irradiated for 4 hr., yielded only carbonyl fluoride, silicon tetrafluoride, and carbon dioxide. Spectroscopic examination of the very small amount (<2%) of gas remaining after treatment with aqueous sodium hydroxide showed that it was not chlorotrifluoromethane, hexafluoroethane, or trifluoroiodomethane.

Halogen-sensitised Oxidation of Heptafluoroiodopropane.—Heptafluoroiodopropane (0·550 g., 0·00185 mole), oxygen (0·256 g., 0·008 mole), and chlorine (0·069 g., 0·00097 mole), sealed in a 150-ml. silica tube (liquid phase present; initial pressure *ca.* 2 atm.) and irradiated for 90 min., deposited iodine and iodine monochloride on the walls of the tube. The condensable products were shaken with an excess of mercury in a sealed tube to remove free halogens and then distilled *in vacuo* to give (*a*) unchanged heptafluoroiodopropane (0·044 g., 0·00015 mole, 8%); (*b*) a fraction (0·00029 mole) comprising 80% pentafluoropropionyl fluoride, heptafluoroiodopropane, and a small amount of an unidentified material (trifluoroacetyl fluoride, chloropentafluoroethane, and chloroheptafluoropropane were absent); (*c*) a fraction (0·00023 mole) comprising pentafluoropropionyl fluoride (90%) and trifluoroacetyl fluoride (10%), with no carbonyl chlorofluoride; and (*d*) a fraction (0·00394 mole) comprising carbonyl fluoride, carbon dioxide, and silicon tetrafluoride; chlorotrifluoromethane was absent, since the fraction was completely absorbed by aqueous sodium hydroxide. These fractions were analysed spectroscopically. The yield of pentafluoropropionyl fluoride (0·00044 mole) is thus 24% and of trifluoroacetyl fluoride (0·000023 mole) is 1%.

Experiments carried out with heptafluoroiodopropane (0·550 g., 0·00185 mole) and oxygen (0·256 g., 0·008 mole) in the reaction vessel used in the last experiment and with comparable conditions and techniques but with bromine as sensitiser are shown in Table 3. The carboxylic acid was converted into its silver salt for identification.

Compounds of Type $CF_3{\cdot}[CF_2]_n{\cdot}CFCl_2$.—*1 : 1-Dichlorohexafluoropropane.* Reaction of 1-chloro-1-iodohexafluoropropane with an excess of chlorine at 60° in the dark (48 hr.) (cf. *J.*, 1953, 1592) gave a quantitative yield of dichlorohexafluoropropane, purified *in vacuo* (Found: *M*, 221. Calc. for $C_3Cl_2F_6$: *M*, 221).

Irradiation for 6 hr. of 1 : 1-dichlorohexafluoropropane (0·440 g., 0·00199 mole) and oxygen (0·008 mole) in a 180-ml. silica tube caused only 2% decomposition.

In a second experiment, dichlorohexafluoropropane (0·435 g., 0·00197 mole) and oxygen (0·008 mole) in a 150-ml. silica tube, irradiated for 28 hr., gave unchanged dichloro-compound (62%), pentafluoropropionyl fluoride (21%), trifluoroacetyl fluoride (2%), and the usual mixture of breakdown products.

Compounds of Type $CF_3{\cdot}[CF_2]_n{\cdot}CFClBr$.—(a) *1-Bromo-1-chlorohexafluoropropane.* 1-Chloro-1-iodohexafluoropropane (1·77 g., 0·0057 mole; prepared as described in *J.*, 1953, 1592) and bromine (2·00 g., 0·0125 mole) were sealed in a 50-ml. silica tube which was shaken, exposed to ultraviolet light for 6 hr., then kept in the dark (5 days). The excess of bromine was removed from the volatile products by reaction with mercury in a sealed tube, and fractionation *in vacuo* gave unchanged 1-chloro-1-iodohexafluoropropane (0·28 g., 16%) and *1-bromo-1-chlorohexafluoropropane* (0·9556 g., 0·00366 mole, 64%), b. p. (isoteniscope) 54° (Found: C, 13·3%; *M*, 265. C_3BrClF_6 requires C, 13·5%; *M*, 265).

1-Bromo-1-chlorohexafluoropropane (0·5865 g., 0·0022 mole) and oxygen (0·2816 g., 0·0088 mole) were sealed in a 50-ml. silica tube (liquid phase present; initial pressure *ca.* 4·7 atm.) which was shaken and irradiated for 30 min.; 3% of the bromo-compound was oxidised to carbonyl fluoride, carbon dioxide, and silicon tetrafluoride. The experiment repeated with an irradiation time of 10 hr. gave 60% of unchanged bromo-compound; pentafluoropropionyl fluoride (45%) and trifluoroacetyl fluoride (8%) were formed and identified spectroscopically before hydrolysis and conversion into salts for analysis. A further experiment using weights of reactants as above but with the addition of bromine and water (2 ml.) is summarised in Table 3.

For comparison of reaction rates, 1-chloro-1-iodohexafluoropropane (0·6886 g., 0·0022 mole) and oxygen (0·2816 g., 0·0088 mole) were sealed in a 50-ml. silica tube identical with that used in the last experiment (liquid phase present; initial pressure *ca.* 4·6 atm.) and shaken by the

side of the tube containing the 1-bromo-1-chlorohexafluoropropane. After 30 minutes' irradiation under the same conditions as used for the bromo-compound, 1-chloro-1-iodohexafluoropropane had undergone oxidation to an extent of 35% to give carbonyl fluoride, carbon dioxide, silicon tetrafluoride, and pentafluoropropionyl fluoride (0·088 g., 0·00053 mole). The oxidation under the conditions specified above gives a 69% yield (24% conversion) of the acyl fluoride; the slower rate of oxidation of the iodo-compound compared with that under the conditions given below (see also Table 2) is caused by the difference in pressure.

(b) *Bromochlorodifluoromethane.* This compound [0·2530 g., 0·00153 mole, prepared as described earlier (*J.*, 1952, 4259)] was condensed with oxygen (0·3200 g., 0·010 mole) into a previously evacuated 50-ml. silica tube. At reaction temperature there was no liquid phase and the initial pressure was *ca.* 5·8 atm. Reddish-yellow vapours were produced on irradiation, and after 6·5 hr., distillation of the reaction products gave crude bromochlorodifluoromethane, which was shaken with 20% aqueous sodium hydroxide to remove halogen then redistilled to give the unchanged bromochlorodifluoromethane (0·1058 g., 0·00064 mole, 42%). Bromochlorodifluoromethane is stable to aqueous sodium hydroxide. The more volatile products (carbonyl halides, silicon tetrafluoride, free halogens, etc., identified by infrared spectroscopic examination) were completely decomposed by 20% aqueous sodium hydroxide.

Experiments carried out under strictly comparable conditions are shown in Table 4, and reveal the effect of variation of reactant ratio under constant pressure and of variation of initial pressure with constant reactant ratio. A 150-ml. silica tube was used, and the reactants, which were completely in the vapour phase, were irradiated for 6·5 hr.

TABLE 4.

CF_2ClBr: g.	mole	O_2 g.	mole	Ratio $O_2 : CF_2ClBr$	Initial pres. (atm.)	Oxidation (%)
0·768	0·00464	0·994	0·0310	7	6	80
0·151	0·00091	0·199	0·00622	7	1	99
0·511	0·00309	0·129	0·00404	1·3	1	87

Compounds of Type $CF_2{\cdot}[CF_2]_n{\cdot}CFClI$. *1-Chloro-1-iodohexafluoropropane.* This compound was prepared from chlorotrifluoroethylene by reaction with trifluoroiodomethane (Haszeldine and Steele, *J.*, 1953, 1592) or with trifluoroacetyl iodide (unpublished work). It was distilled *in vacuo* before use, and was spectroscopically pure and peroxide-free.

(i) Photochemical oxidation. 1-Chloro-1-iodohexafluoropropane (0·756 g., 0·00242 mole) and oxygen (0·3072 g., 0·0096 mole) in a 150-ml. silica tube (liquid phase present; initial pressure *ca.* 1·8 atm.) were irradiated and shaken until no liquid phase remained (25 min.). Iodine was deposited on the walls of the tube. The products were distilled to give (*a*) unchanged 1-chloro-1-iodohexafluoropropane (0·1843 g., 0·00059 mole; 24%), (*b*) carbonyl fluoride, carbon dioxide, and silicon tetrafluoride (0·00057 mole), (*c*) trifluoroacetyl fluoride (0·007 g., 0·00005 mole, 2% conversion), and (*d*) *pentafluoropropionyl fluoride* (0·1975 g., 0·00119 mole, 49% conversion), b. p. −26·5° (isoteniscope) (Found: C, 21·3%; equiv., 85; *M*, 165. C_3OF_6 requires C, 21·7%; equiv., 83; *M*, 166). The yields of pentafluoropropionyl fluoride and trifluoroacetyl fluoride were 65 and 3%, respectively. Trifluoroacetyl fluoride was identified by means of its infrared spectrum; the spectrum of pentafluoropropionyl fluoride revealed the acyl carbonyl band.

1-Chloro-1-iodohexafluoropropane (0·758 g., 0·00243 mole) and oxygen (0·801 g., 0·025 mole) in a 150-ml. silica tube (initial pressure *ca.* 4·6 atm.) were irradiated under conditions identical with those for the first reaction to give unchanged iodo-compound (65%), pentafluoropropionyl fluoride (59%), trifluoroacetyl fluoride (4%), and a mixture of carbon dioxide, silicon tetrafluoride, and carbonyl fluoride.

(ii) Dark reaction. 1-Chloro-1-iodohexafluoropropane (0·380 g., 0·0012 mole) and oxygen (0·1056 g., 0·0033 mole) in a sealed 50-ml. Pyrex tube (liquid phase present; initial pressure *ca.* 1·8 atm.) were shaken in complete darkness for 33 days. Less than 0·05% of oxidation (based on the absence of volatile products) had then occurred. The unchanged iodo-compound was removed by pumping, leaving a small amount of a white solid in the tube. This solid, which is believed to be a peroxide, decomposed when exposed to dry air and liberated iodine.

(iii) Photochemical oxidation in presence of water. A 150-ml. silica tube containing 1-chloro-1-iodohexafluoropropane (0·596 g., 0·00191 mole), oxygen (0·3072 g., 0·0096 mole, initial pressure *ca.* 1·8 atm.), and water (2·5 ml.) was shaken and irradiated for 4·5 hr. Iodine was deposited and the organic layer disappeared. The only volatile product was carbon dioxide (0·0135 g., 0·000307 mole, 16%). The aqueous solution was shaken with mercury to remove iodine and then treated with a slight excess of silver carbonate. The filtered solution was evaporated

to dryness, and the residual solid extracted several times with dry ether. The ethereal extracts were evaporated to give a mixture of silver salts (0·3381 g.). Analysis of the mixture by means of infrared spectroscopy showed it to contain only silver trifluoroacetate and pentafluoropropionate in the ratio 1 : 5. The yield of silver pentafluoropropionate (0·282 g.) is thus 55%, and of silver trifluoroacetate (0·056 g.) 13%.

(iv) Halogen-sensitised oxidation. The last experiment was repeated, with the addition of chlorine (0·71 g., 0·010 mole) to the reaction mixture. The products were treated as above, and yielded silver trifluoroacetate (18%) and silver pentafluoropropionate (73%).

A 150-ml. tube containing 1-chloro-1-iodohexafluoropropane (0·601 g., 0·00192 mole), oxygen (0·310 g., 0·0097 mole; initial pressure *ca.* 1·8 atm.), and bromine (0·402 g., 0·0025 mole) was irradiated for 0·5 hr. to give unchanged iodo-compound (10%), pentafluoropropionyl fluoride (69%), trifluoroacetyl fluoride (21%), and breakdown products.

Photochemical Oxidation of Pentafluoropropionyl Fluoride.—The acyl fluoride (0·1368 g., 0·000824 mole) and oxygen (0·1146 g., 0·00358 mole, pressure *ca.* 0·74 atm.) in a 150-ml. silica tube were irradiated for 65 min. Distillation of the condensable products *in vacuo* gave unchanged pentafluoropropionyl fluoride (0·1145 g., 0·00069 mole, 84%) and carbon dioxide, silicon tetrafluoride, and carbonyl fluoride. Infrared spectroscopic examination showed no trifluoroacetyl fluoride.

Irradiation for 21 days of a mixture of pentafluoropropionyl fluoride (0·1610 g., 0·00097 mole) and oxygen (0·1146 g., 0·00358 mole, pressure *ca.* 0·77 atm.) caused complete oxidation to carbon dioxide and silicon tetrafluoride. Spectroscopic examination showed that trifluoroacetyl fluoride and carbonyl fluoride were absent.

Compounds of Type $F\cdot[CF_2]_n\cdot CFBr_2$.—*Dibromodifluoromethane.* This compound (see *J.*, 1952, 4259) (0·3192 g., 0·00152 mole) and oxygen (0·3200 g., 0·010 mole) in a 50-ml. silica tube (pressure *ca.* 5·6 atm.) were exposed to ultraviolet light (6·5 hr.) to give products heavily contaminated with free bromine. After removal of bromine, carbonyl halides, etc., by treatment with 20% aqueous sodium hydroxide, only 2% of the dibromodifluoromethane was recovered unchanged. Dibromodifluoromethane is stable towards 20% aqueous sodium hydroxide under the conditions used.

The experiment was repeated with an irradiation time of 4 hr.; 88% of the dibromodifluoromethane had then decomposed.

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The Chemistry of Fungi. Part XXV. Oosporein, a Metabolite of* Chaetomium aureum *Chivers.*

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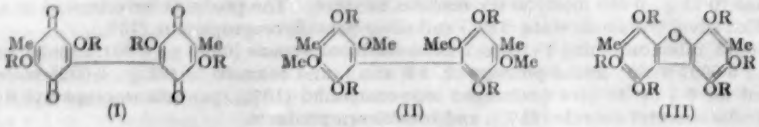
The polyhydroxy-diphenyldiquinone, oosporein (I; R = H) (Kögl and van Wessem, *Rec. Trav. chim.*, 1944, **63**, 5), has been isolated from a strain of *Chaetomium aureum* Chivers and derivatives have been prepared.

DURING a comprehensive investigation of the metabolites from the *Chaetomium* genus, a copper-coloured pigment, $C_{14}H_{10}O_8$, was isolated from the mycelium and the metabolic liquors of a strain of *Chaetomium aureum* Chivers, grown on a modified William Saunders medium. This pigment exhibited properties typical of a polyhydroxyquinone, being readily converted into a tetra-acetate, $C_{14}H_6O_4(OAc)_4$ and reductively acetylated to an octa-acetate, $C_{14}H_6(OAc)_8$. The close correspondence between the properties of the metabolite and of the two acetates with oosporein (Kögl and van Wessem, *Rec. Trav. chim.*, 1944, **63**, 5) (I; R = H) and its appropriate derivatives indicated identity. A direct comparison

* Part XXIV, *J.*, 1955, 11.

between the three substances kindly supplied by Professor F. Kögl and the products obtained by us, including a comparison of their infrared absorption spectra, confirmed this.

Methylation of oosporein with a large excess of diazomethane gave the tetramethyl ether (I; R = Me) which was readily reduced to tetrahydrotetra-*O*-methyloosporein (II; R = H). Reductive acetylation of tetra-*O*-methyloosporein (I; R = Me) furnished



(I) (II) (III)

tetra-*O*-acetyltetrahydrotetra-*O*-methyloosporein (II; R = Ac), identical with the acetylation product of tetrahydrotetra-*O*-methyloosporein. Methylation of the tetrahydric phenol (II; R = H), obtained by the catalytic hydrogenation of tetra-*O*-methyloosporein, by either the methyl sulphate or the methyl iodide–potassium carbonate method furnished a mixture of tetrahydro-octa-*O*-methyloosporein (II; R = Me) and, unexpectedly, the dibenzofuran (III; R = Me), which was readily demethylated. Efforts to convert tetrahydrotetra-*O*-methyloosporein into a dibenzofuran of type (III) by dehydration with the usual reagents were uniformly unsuccessful (cf. Part XXIV, *loc. cit.*).

Experimental

(With D. H. Johnson) *Isolation of Oosporein.*—The mould *Chaetomium aureum* Chivers was grown on a modified William Saunders medium, containing glucose (50 g.), glycine (2 g.), potassium dihydrogen phosphate (2 g.), calcium chloride (0·5 g.), malt extract (1·4 g.), ammonium sulphate (0·3 g.), magnesium sulphate (0·25 g.), boric acid (0·5 g.), ferric chloride (0·25 g.), thallous chloride (0·5 g.), potassium iodide (0·05 g.), copper sulphate (0·05 g.), manganous chloride (0·5 g.), and zinc sulphate (0·5 g.; all quantities per l.) at 25° for 21 days. The mycelial felts were collected, dried, powdered, and exhaustively extracted (Soxhlet) with light petroleum (b. p. 40—60°) for 4 days and then with ether; a part of the pigment separated in a state of high purity in the Soxhlet boiler. The metabolic liquid was concentrated in a vacuum to about one-tenth of its volume. Several days later the brown precipitate (*ca.* 10 g., from 180 l. of metabolic fluid) was collected, dried, and repeatedly extracted with boiling acetone (1 l.), and the extract reduced by distillation (to about 30 ml.), oosporein then separating as bronze plates. The combined yield of pigment from mycelium and liquor varied from 0·02 to 0·11 g. per l. of culture fluid, and the relative distribution between metabolic liquid and mycelium also varied widely. Growth of the mould at 30° did not appear to alter the yield of metabolite materially but at room temperature (*ca.* 15—16°) the yield was considerably lower; when glucose was replaced by glycerol the organism did not produce the pigment. Thus obtained, oosporein separated from acetone–light petroleum (b. p. 60—80°) in bronze-coloured plates, m. p. 260—275° (decomp.) (Found: C, 55·0; H, 3·7. Calc. for $C_{14}H_{10}O_8$: C, 54·9; H, 3·3%).

Oosporein tetra-acetate crystallised from ethyl acetate–light petroleum (b. p. 60—80°) in yellow needles, m. p. 191° undepressed on admixture with a specimen supplied by Professor F. Kögl; the infrared absorption spectra of the two derivatives were identical [Found: C, 55·9 55·8; H, 3·7, 3·9; OAc, 35·5. Calc. for $C_{14}H_6O_4(OAc)_4$: C, 55·7; H, 3·8; OAc, 36·3%]; Kögl and van Wessem (*loc. cit.*) record m. p. 184°.

Octa-O-acetyltetrahydro-oosporein separated from alcohol in prisms, m. p. 250° [Found: C, 55·8, 55·7; H, 4·7, 4·9; OAc, 46·7. Calc. for $C_{14}H_6(OAc)_8$: C, 55·7; H, 4·7; OAc, 53·3%]. The infrared absorption spectrum of this compound was identical with that of a specimen supplied by Professor Kögl; Kögl and van Wessem (*loc. cit.*) give m. p. 231°.

Methylation of Oosporein.—Ethereal diazomethane (from 12 g. of methylnitrosourea) was rapidly added to oosporein (1 g.) in cold methanol (175 ml.) and 5 min. later the mixture was acidified with 2N-sulphuric acid (2 drops) and concentrated to *ca.* 20 ml. in a vacuum. When precipitated from the concentrate with water (50 ml.), *tetra-O-methyloosporein* was purified from light petroleum (b. p. 60—80°) and then by chromatography from benzene on neutralised alumina, forming orange needles, m. p. 125° [Found: C, 59·7; H, 5·3; OMe, 34·0%; *M*, 360. $C_{14}H_6O_4(OMe)_4$ requires C, 59·7; H, 5·0; OMe, 34·2%; *M*, 362]. This ether is soluble in the

usual organic solvents, insoluble in aqueous 2N-sodium carbonate, and has a negative ferric reaction.

With less diazomethane (*ca.* 4 mol.) methylation furnished two isomeric *trimethyl ethers* of oosporein, *viz.*, (A) which separated from aqueous methanol in golden plates, m. p. 154° [Found: C, 58·2, 58·5; H, 4·9, 4·5; OMe, 26·3, 25·9. $C_{14}H_7O_5(OMe)_3$ requires C, 58·6; H, 4·7; OMe, 26·7%], and (B) forming yellow plates, m. p. 192°, from aqueous methanol (Found: C, 58·1; H, 4·4; OMe, 22·5%), a mixture of the two melting at 130—142°. The compounds, which gave blood-red ferric reactions in alcohol, formed deep purple solutions in aqueous 2N-sodium hydrogen carbonate from which they were recovered unchanged on acidification. Treatment of ether (A) or (B) with an excess of diazomethane gave an almost quantitative yield of tetra-*O*-methyloosporein.

Tetrahydro-octa-O-methyloosporein.—Tetra-*O*-methyloosporein (3 g.), dissolved in methanol (150 ml.), was hydrogenated with a palladium–charcoal catalyst (from 2 g. of charcoal and 0·2 g. of palladium chloride) for 30 min. (absorption, 304 ml.; calc. for 2 mol., 370 ml.). Removal of the solvent in a vacuum left *tetrahydrotetra-O-methyloosporein* which separated from aqueous methanol in needles (2·2 g.), m. p. 197°, readily soluble in aqueous 2N-sodium hydroxide and having a negative ferric reaction in alcohol [Found: C, 58·9; H, 5·9; OMe, 33·5. $C_{14}H_{10}O_4(OMe)_4$ requires C, 59·0; H, 6·0; OMe, 33·8%]. The same product was obtained by the reduction of tetra-*O*-methyloosporein in methanol with sulphur dioxide.

Acetylation of tetrahydrotetra-*O*-methyloosporein (0·2 g.) with acetic anhydride (5 ml.) and concentrated sulphuric acid (2 drops) on the steam-bath for 15 min. furnished *tetra-O-acetyltetrahydrotetra-O-methyloosporein* which crystallised from aqueous acetic acid in needles (0·18 g.), m. p. 146°, identical with the product formed by the reductive acetylation of tetra-*O*-methyloosporein. This compound was insoluble in aqueous 2N-sodium hydroxide and had a negative ferric reaction in alcohol (Found: C, 58·3; H, 5·5. $C_{26}H_{30}O_{12}$ requires C, 58·4; H, 5·6%).

When tetrahydrotetra-*O*-methyloosporein (1 g.) was methylated by either methyl sulphate or methyl iodide–potassium carbonate–acetone for 6 hr., the product was almost invariably a mixture (0·8 g.), m. p. 130—140°, which was separated by fractional crystallisation from methanol into 1 : 3 : 4 : 5 : 6 : 8-*hexamethoxy*-2 : 7-*dimethyldibenzofuran*, plates, m. p. 141—142° [Found: C, 64·0; H, 6·5; OMe, 49·2%; *M*, 374. $C_{14}H_6O(OMe)_6$ requires C, 63·9; H, 6·4; OMe, 49·0%; *M*, 376], and *tetrahydro-octa-O-methyloosporein*, octahedra, m. p. 179° [Found: C, 63·0; H, 7·1; OMe, 57·4. $C_{14}H_8(OMe)_8$ requires C, 62·6; H, 7·1; OMe, 58·7%]. These products had negative ferric reactions and were insoluble in aqueous 2N-sodium hydroxide.

Demethylation of 1 : 3 : 4 : 5 : 6 : 8-hexamethoxy-2 : 7-dimethyldibenzofuran (0·5 g.) with a boiling mixture of hydriodic acid (10 ml.; *d* 1·7) and acetic acid (from 5 ml. of anhydride) for 10 min. and dilution with water furnished 1 : 3 : 4 : 5 : 6 : 8-hexahydroxy-2 : 7-dimethyldibenzofuran which separated from methanol in needles, m. p. 300° (decomp.), and on exposure to air rapidly oxidised. On acetylation with acetic anhydride–sulphuric acid this unstable phenol gave 1 : 3 : 4 : 5 : 6 : 8-*hexa-aceloxy*-2 : 7-*dimethyldibenzofuran*, forming prisms, m. p. 274°, from methanol [Found: C, 57·6; H, 4·6; OAc, 43·1. $C_{14}H_8O(OAc)_8$ requires C, 57·4; H, 4·5; OAc, 47·4%]. Methylation of the phenol by methyl sulphate–potassium carbonate regenerated the parent ether, m. p. and mixed m. p. 141—142°.

UNIVERSITY OF LIVERPOOL. [*Received, March 4th*, 1955.]

Usnic Acid. Part XI. A Synthesis of 7-Acetyl-4 : 6-dihydroxy-3 : 5-dimethylcoumaran-2-one.*

By F. M. Dean and Alexander Robertson.

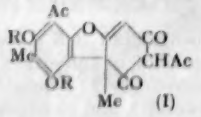
[Reprint Order No. 6196.]

7-Acetyl-4 : 6-dihydroxy-3 : 5-dimethylcoumaran-2-one (II; R = H), identical with the ozonolysis product from usnic acid (Schöpf and Ross, *Annalen*, 1941, **546**, 1), has been synthesised from methyl 4 : 6-dimethoxy-3 : 7-dimethylcoumarilate.

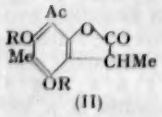
In exploratory experiments dihydropyran was found to react at the 6-position of 5 : 7-dihydroxy-4 : 8-dimethylcoumarin and did not form the expected ether.

Phloroglucinol trimethyl ether and *C*-methylphloracetophenone respectively condense with ethyl α-chloro-α-ethoxyacetate to give only diphenylacetates with the simultaneous elimination of alcohol and hydrogen chloride.

The observation by Schöpf and Ross (*Annalen*, 1941, **546**, 1) that ozonolysis of di-*O*-acetylusnic acid (I; R = Ac) gives rise to the lactone (II; R = Ac) serves to substantiate the structure (I; R = H) for usnic acid proposed by Curd and Robertson (*J.*, 1937, 894). Whilst the mode of formation and the properties of the diacetate (II; R = Ac) described by Schöpf and Ross (*loc. cit.*), Asahina and Okazaki (*J. Pharm. Soc. Japan*, 1943, **63**, 618), and Barton and Bruun (*J.*, 1953, 603) place its constitution beyond doubt, a synthesis of this compound has not hitherto been described. The dihydric phenol formed by deacetylation of this diacetate (II; R = Ac) was considered by the German authors to be the rearranged product (III; R = H) rather than the direct product (II; R = H) because on reacetylation it furnished a diacetate different from the original. Asahina and Okazaki (*loc. cit.*), however, showed that the compounds were dimorphic and hence the phenol (II; R = H) is apparently formed preferentially to its isomer (III; R = H) when the acid (IV) lactonises.



(I)



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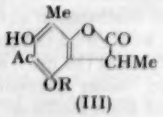

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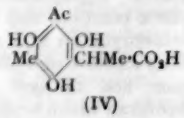


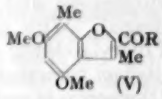
(IV)

Although slow in boiling alcohol or toluene, the formation of the hydrazide (V; R = $NH{\cdot}NH_2$) from methyl 4 : 6-dimethoxy-3 : 7-dimethylcourmarilate (V; R = OMe) was rapid in hot Carbitol (diethylene glycol monomethyl ether). This hydrazide was converted by the Curtius method into the urethane (VI) for which the alternative structure (VII) is also possible. In support of formula (VI) the infrared spectrum of the compound showed absorption at 3360 cm.$^{-1}$, characteristic of amidic :NH group. On vigorous alkaline hydrolysis or selective dealkylation with hydriodic acid this comparatively stable urethane gave 4 : 6-dimethoxy-3 : 7-dimethylcoumaran-2-one (VIII) exhibiting the strong absorption at 1802 cm.$^{-1}$, typical of $\beta\gamma$-unsaturated five-membered lactones; the corresponding hydroxy-acid was not isolated.

C-Acetylation of the lactone (VIII) with acetic anhydride and boron trifluoride gave a lactone which had the properties of an *o*-hydroxy-ketone, showing that monodemethylation had occurred (cf. Part VIII, *J.*, 1953, 1241) but it was not obvious which methoxyl group had survived. In keeping with the fact that it is not identical with the phenol (X; R = Me) formed by the partial methylation of the phenol (II; R = H) and is not isomerised on hydrolysis this lactone is provisionally regarded as having formula (III; R = Me). The other possible structure (IX) for this compound might be expected to permit the isomerisation in view of the tendency of the acid (IV) to regenerate the phenol (II; R = H)

* Part X, *J.*, 1954, 4565.

under similar conditions (cf. Asahina and Okazaki, *loc. cit.*). With the common demethylating agents, *e.g.*, hydriodic and hydrobromic acid or aluminium chloride, the lactone (III; R = Me) was completely destroyed but on being heated with magnesium iodide (cf. Schönberg and Sina, *J. Amer. Chem. Soc.*, 1950, **72**, 3396) it gave a small yield of a demethylation product which was identical with the lactone (II; R = H) from usnic acid,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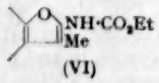
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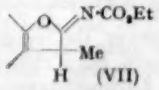
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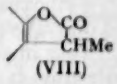
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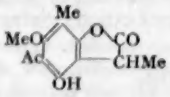
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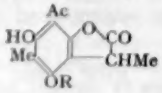
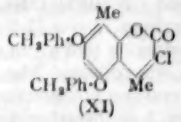

(X)

having the same infrared absorption spectrum. As the method employed to isolate the synthetic lactone (II; R = H) was of a hydrolytic nature this would clearly allow the formation of the acid (IV) and consequently the production of the lactone (II; R = H).

Acetylation of the natural or the synthetic lactone (II; R = H) by the method of Schöpf and Ross (*loc. cit.*) gave only the monoacetate (X; R = Ac) and not the expected diacetate (II; R = Ac), a result which seems to be due to the ease with which the diacetate is partially hydrolysed in the isolation process. Shibata, Asahina, and Takahaski (*J. Pharm. Soc. Japan*, 1952, **72**, 255) obtained this monoacetate * by pyrolysis of (+)-diacetyldihydrousnic acid and identified it with the product formed by the partial deacetylation of the diacetate (II; R = Ac).

In attempts to avoid the unsatisfactory demethylation process other routes to the phenol (II; R = H) were explored which, however, did not appear promising. With sodium hydroxide the dibenzyl ether (XI) gave 4 : 6-dibenzyloxy-3 : 7-dimethylcoumarilic acid (XII; R = OH). The hydrazide (XII; R = $NH{\cdot}NH_2$) was obtained from the methyl ester (XII; R = OMe) of this acid, and on treatment with nitrous acid and then with the appropriate alcohol furnished the urethanes (XIII; R = Et) and (XIII; R = CH_2Ph) which on attempted hydrolysis gave only resins.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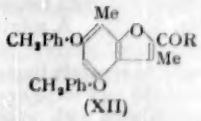
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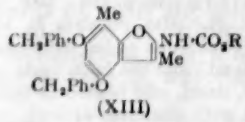
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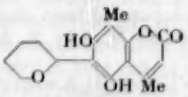
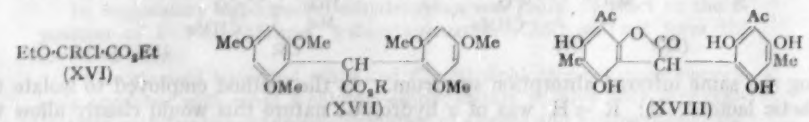

(XIV)

(XV)

The formation of 2-tetrahydropyranyl ethers has been employed by Parker and Anderson (*J. Amer. Chem. Soc.*, 1948, **70**, 4187) and Geissman (*ibid.*, 1951, **73**, 3514) (cf. Woods and Kramer, *ibid.*, 1947, **69**, 2246) for the protection of phenolic hydroxyl groups but under the conditions described 5 : 7-dihydroxy-4 : 8-dimethylcoumarin failed to react with dihyropyran. With more drastic conditions a phenolic adduct was obtained which, since it did not react with diazonium salts and formed a dimethyl ether stable to acid hydrolysis, is considered to have the formula (XIV). This type of addition to dihydropyran does not appear to have been observed previously but may be regarded as an extension of the well-established Friedel–Crafts reaction with simpler olefins here facilitated by the strongly anionoid nature of the phloroglucinol residue. Because the active intermediate is presumably (XV) the 2- rather than the 3-position of the pyran system is believed to be involved.

* The Japanese authors attribute the isolation of this monoacetate to Schöpf and Ross (*loc. cit.*) who, however, do not refer to it in their communication.

Quelet and Gavarret (*Compt. rend.*, 1950, **250**, 394) have shown that the interaction of ethyl α-chloro-α-ethoxyacetate (XVI; R = H) and the methyl ethers of phenols gives the α-chloro-α-arylacetates, $Ar{\cdot}CHCl{\cdot}CO_2Et$, along with small amounts of diarylacetates, $Ar_2CH{\cdot}CO_2Et$, by a secondary reaction. Hydrogenolysis of the chloro-esters $Ar{\cdot}CHCl{\cdot}CO_2Et$ furnished good yields of the corresponding arylacetates and accordingly a synthesis of the phenol (II; R = H) from *C*-methylphloracetophenone and ethyl α-chloro-α-ethoxyacetate (XVI; R = H) in two steps was envisaged. With phloroglucinol derivatives, however, the secondary reaction (formation of diarylacetates) supervened. Thus in acetic acid, ethyl chloroethoxyacetate and phloroglucinol trimethyl ether gave only ethyl di-(**2 : 4 : 6**-trimethoxyphenyl)acetate (XVII; R = Et) whereas in methanol a slower reaction was accompanied by trans-esterification, giving the analogous ester



(XVII; R = Me). In ether, in which the condensation was very slow, the required product, $Ar{\cdot}CHCl{\cdot}CO_2Et$, was not obtained even when the reaction was interrupted whilst much unchanged phloroglucinol trimethyl ether was still present. With *C*-methylphloracetophenone and the ester (XVI; R = H) a diaryl derivative was obtained which was devoid of a methoxyl group and formed a penta-acetate. This compound is considered to have a structure of type (XVIII), where the orientation of the lactone system conforms with the behaviour of the simpler diphenol (II; R = H). Phloroglucinol triacetate and the ester (XVI; R = H) did not react at room temperature and on being heated gave a resin.

Experimental

*2-Ethoxycarbonylamino-***4** : **6**-*dimethoxy-***3** : **7**-*dimethylcoumarone* (VI).—A mixture of methyl **4** : **6**-dimethoxy-**3** : **7**-dimethylcoumarilate (Part X, *J.*, 1954, 4565) (**1** g.), **90%** hydrazine hydrate (**1·5** ml.), and Carbitol (**10** ml.) was heated under reflux for **1** hr., cooled, and diluted with water (**50** ml.). The resulting *hydrazide* (V; R = $NH{\cdot}NH_2$) crystallised from alcohol in needles (**1·7** g.), m. p. **208**—**210°**, which reduced Fehling's solution [Found : N, **10·7**; OMe, **24·0**. $C_{11}H_{10}O_2N_2(OMe)_2$ requires N, **10·6**; OMe, **23·5%**]. A solution of sodium nitrite (**1·5** g.) in water (**5** ml.) was added dropwise to a well-stirred mixture of this hydrazide (**5·3** g.) in acetic acid (**80** ml.) and the fawn azide, which began to separate immediately, was collected **2** hr. later, washed, dried, and heated in boiling alcohol (**50** ml.) for **2** hr. The resulting hot solution was treated with charcoal, filtered, cooled, and diluted with water, giving *2-ethoxycarbonylamino-***4** : **6**-*dimethoxy-***3** : **7**-*dimethylcoumarone* (VI) which separated from alcohol or benzene in colourless needles (**4** g.), m. p. **150**—**151°** (Found : C, **61·0**; H, **6·6**; N, **5·0**. $C_{15}H_{19}O_5N$ requires C, **61·4**; H, **6·6**; N, **4·8%**).

4 : **6**-*Dimethoxy-***3** : **7**-*dimethylcoumaran-***2**-*one* (VIII).—(*A*) A solution of the aforementioned urethane (VI) (**1** g.) in a mixture of acetic acid (**20** ml.) and hydriodic acid (**10** ml.; *d* **1·7**) was boiled for **1·5** hr. On cooling, the mixture deposited a crystalline solid (**0·5** g.) which on purification from alcohol gave **4** : **6**-*dimethoxy-***3** : **7**-*dimethylcoumaran-***2**-*one* in prisms, m. p. **125°** [Found : C, **64·6**; H, **6·3**; OMe, **27·9**. $C_{10}H_8O_3(OMe)_2$ requires C, **64·9**; H, **6·4**; OMe, **27·9%**]. This compound, which was insoluble in cold aqueous **2N**-sodium hydroxide, dissolved in the hot reagent and the solution gave an intense blue colour with Gibbs's reagent.

(*B*) On being heated with potassium hydroxide (**0·8** g.) in boiling Carbitol (**40** ml.) the urethane (VI) rapidly liberated ammonia and **10** min. later the mixture was cooled, diluted with water (**200** ml.), and acidified with concentrated hydrochloric acid. The resulting precipitate of coumaran-2-one (VIII) crystallised from acetic acid in prisms (**0·5** g.), m. p. and mixed m. p. **125°**.

*5-Acetyl-***6**-*hydroxy-***4**-*methoxy-***3** : **7**-*dimethylcoumaran-***2**-*one* (III; R = Me).—A rapid stream of boron trifluoride (from **40** g. of potassium fluoroborate) was led into a solution of **4** : **6**-dimethoxy-**3** : **7**-dimethylcoumaran-2-one (**1** g.) in acetic acid (**10** ml.) containing acetic anhydride (**10** ml.). After **40** min. the addition of water (**200** ml.) to the cooled mixture precipitated a sticky yellow mass which was dissolved in ether. This solution was washed with

much water and on evaporation gave *5-acetyl-4-methoxy-6-hydroxy-3 : 7-dimethylcoumaran-2-one* which formed pale yellow prisms (0·4 g.), m. p. 127°, from alcohol, with a dark violet ferric reaction; the yellow solution of the coumaran-2-one in aqueous sodium hydroxide gave a negative Gibbs's reaction (Found : C, 62·3; H, 5·6; OMe, 12·6. $C_{13}H_{11}O_4$·OMe requires C, 62·4; H, 5·6; OMe, 12·4%). This compound was not affected by aqueous N-sodium hydroxide at 90° for 1·5 hr.

7-Acetyl-6-hydroxy-4-methoxy-3 : 5-dimethylcoumaran-2-one (X; R = Me).—7-Acetyl-4 : 6-dihydroxy-3 : 5-dimethylcoumaran-2-one (Schöpf and Ross, *loc. cit.*) (0·2 g.) was heated with methyl iodide (0·1 ml.) and potassium carbonate (0·5 g.) in boiling acetone (50 ml.) for 4 hr. On isolation the resulting *7-acetyl-6-hydroxy-4-methoxy-3 : 5-dimethylcoumaran-2-one* separated from methanol in prisms, m. p. 178°, with a greenish-red ferric reaction in dilute alcohol (Found : C, 62·2; H, 5·4; OMe, 12·0. $C_{13}H_{11}O_4$·OMe requires C, 62·4; H, 5·6; OMe, 12·4%).

7-Acetyl-4 : 6-dihydroxy-3 : 5-dimethylcoumaran-2-one (II; R = H).—A solution of 5-acetyl-6-hydroxy-4-methoxy-3 : 7-dimethylcoumaran-2-one (0·2 g.) in benzene, containing magnesium iodide (0·5 g.), was evaporated and the residue kept at 180° for 40 min. The red mass was extracted several times with hot dilute sulphuric acid and, on cooling, the extracts deposited the crude coumaranone (II; R = H); a further quantity was isolated from the residual red resin with methanol. From methanol, 7-acetyl-4 : 6-dihydroxy-3 : 5-dimethylcoumaran-2-one formed pinkish prisms (*ca.* 10 mg.), m. p. 212°, undepressed on admixture with a natural specimen (Schöpf and Ross, *loc. cit.*) and having a dark blue ferric reaction. Acetylation of this coumaran-2-one (synthetic or natural) by the method of Schöpf and Ross (*loc. cit.*) gave 4-acetoxy-7-acetyl-6-hydroxy-3 : 5-dimethylcoumaran-2-one which separated from methanol in pale yellow needles, m. p. 189—190° having a greenish-red ferric reaction and giving a yellow solution with dilute aqueous sodium hydroxide (Found : C, 60·4; H, 5·2. Calc. for $C_{14}H_{14}O_6$: C, 60·4; H, 5·0%).

Methyl 5 : 7-Dibenzyloxy-3 : 7-dimethylcoumarilate (XII; R = OMe).—3-Chloro-5 : 7-dihydroxy-4 : 8-dimethylcoumarin (Part X, *loc. cit.*) was dried in a vacuum at 150° for 4 hr. and then heated with benzyl bromide (7 g.) and potassium carbonate (6 g.) in boiling acetone (150 ml.) for 10 hr. The resulting *5 : 7-dibenzyloxy-3-chloro-4 : 8-dimethylcoumarin* (XI) crystallised from alcohol in prisms (7 g.), m. p. 220—221° (Found : C, 71·4; H, 4·9; Cl, 8·6. $C_{25}H_{21}O_4Cl$ requires C, 71·3; H, 5·0; Cl, 8·4%).

On being heated with potassium hydroxide (1·2 g.) in boiling Carbitol (30 ml.) for 5 min. this coumarin (4 g.) was converted into the *hydrate* of 4 : 6-dibenzyloxy-3 : 7-dimethylcoumarilic acid (XII; R = OH) which was precipitated from the cooled hydrolysate by hydrochloric acid and purified from dioxan, forming diamond-shaped plates (3 g.), m. p. 210° (decomp.), with a deep red sulphuric acid (warm) reaction (Found : C, 71·4; H, 6·0. $C_{25}H_{22}O_5.H_2O$ requires C, 71·4; H, 6·2%). Formed by use of diazomethane, the *methyl ester* (XII; R = OMe) separated from methanol in prisms, m. p. 116—118° (Found : C, 75·6; H, 6·2; OMe, 7·8. $C_{25}H_{21}O_4$·OMe requires C, 75·0; H, 5·8; OMe, 7·5%).

4 : 6-Dibenzyloxy-2-ethoxycarbonylamino-3 : 7-dimethylcoumarone (XIII; R = Et).—On being heated in boiling Carbitol (100 ml.) with 90% hydrazine hydrate (6 ml.) for 2 hr. methyl 4 : 6-dibenzyloxy-3 : 7-dimethylcoumarilate (13 g.) gave the *hydrazide* (XII; R = NH·NH_2) which separated from alcohol in long prisms (12 g.), m. p. 170°, darkening on exposure to light (Found : N, 6·7. $C_{25}H_{24}O_4N_2$ requires N, 6·7%). Treatment of this hydrazide (4 g.) in acetic acid (70 ml.) with sodium nitrite (0·7 g.) in water (10 ml.) gave the azide which was washed and air-dried. This azide (2 g.) was decomposed with boiling alcohol (15 ml.), the resulting hot solution was treated with charcoal and evaporated, and the residue was chromatographed from benzene on aluminium oxide, giving *4 : 6-dibenzyloxy-2-ethoxycarbonylamino-3 : 7-dimethylcoumarone* which formed needles (0·9 g.), m. p. 144°, from alcohol (Found : N, 3·0; OEt, 11·1. $C_{25}H_{23}O_4N$·OEt requires N, 3·2; OEt, 11·1%).

The crude azide (4 g.) was gently heated with benzyl alcohol (1·1 g.) in toluene (40 ml.) to maintain a steady effervescence and when this had ceased the mixture was boiled for 2 hr., filtered, and evaporated in a vacuum. Crystallised from alcohol, the residue gave the *urethane* (XIII; R = CH_2Ph) in prisms (2·9 g.), which melted at 136° and then on solidification had m. p. 144° (Found : C, 76·0; H, 5·6; N, 3·3. $C_{32}H_{29}O_5N$ requires C, 75·7; H, 5·7; N, 2·8%).

5 : 7-Dihydroxy-4 : 8-dimethyl-6-2′-tetrahydropyranylcoumarin (XIV).—A mixture of 5 : 7-dihydroxy-4 : 8-dimethylcoumarin (Part X, *loc. cit.*) (1·0 g.), dihydropyran (1·4 ml.), and chloroform (8 ml.), containing a trace of sulphuric acid, was kept for 5 days. The grey solid was collected, washed with alcohol, and crystallised from dioxan, giving the *coumarin* (XIV) in colourless prisms (0·3 g.), m. p. 222° (decomp), which formed a yellow solution in aqueous sodium

hydroxide, unchanged on the addition of diazotised sulphanilic acid (Found: C, 66·0; H, 6·6. $C_{16}H_{16}O_5$ requires C, 66·2; H, 6·2%). The *dimethyl ether*, formed by the methyl iodide–potassium carbonate method, had m. p. 150—151° [Found: C, 68·2; H, 7·1; OMe, 18·9%; *M* (Rast), 333. $C_{16}H_{16}O_3(OMe)_2$ requires C, 67·9; H, 7·0; OMe, 19·5%; *M*, 318]. On being boiled with a mixture of alcohol (5 ml.) and 4N-hydrochloric acid (5 ml.) for 1 hr. this dimethyl ether was recovered unchanged.

Ethyl Di-(2 : 4 : 6-trimethoxyphenyl)acetate (XVII; R = Et).—A mixture of ethyl α-chloro-α-ethoxyacetate (2 g.), phloroglucinol trimethyl ether (2 g.), and acetic acid (10 ml.) was kept at 100° for 12 hr.; hydrogen chloride was evolved and the solution became pink. Precipitation with water and purification from alcohol gave *ethyl di-(2 : 4 : 6-trimethoxyphenyl)-acetate* in irregular prisms (1·1 g.), m. p. 158—159·5°, with a negative test for halogen (Found: C, 62·8; H, 6·8. $C_{22}H_{28}O_8$ requires C, 62·9; H, 6·7%).

When the aforementioned mixture was kept at room temperature reaction did not take place but boiling it for 16 hr. gave a product, which was precipitated with water and contained the acetate (XVII; R = Et) (0·2 g.).

Interaction of phloroglucinol trimethyl ether (2 g.) and ethyl α-chloro-α-ethoxyacetate (2 g.) in boiling methanol for 16 hr. gave *methyl di-(2 : 4 : 6-trimethoxyphenyl)acetate* (XVII; R = Me) which separated from light petroleum (b. p. 60—80°) in irregular prisms (1·3 g.), m. p. 147—148° [Found: C, 62·0; H, 6·5; OMe, 53·0. $C_{18}H_{17}O_8(OMe)_3$ requires C, 62·1; H, 6·5; OMe, 53·4%].

7-Acetyl-4 : 6-dihydroxy-5-methyl-3-(3-acetyl-2 : 4 : 6-trihydroxy-5-methylphenyl)-coumar-2-one (XVIII).—On being kept at room temperature for 5 hr. a mixture of *C*-methylphloracetophenone (1·8 g.), ethyl α-chloro-α-ethoxyacetate (1·5 g.), and acetic acid (10 ml.) deposited a yellow solid which could not be recrystallised but which on being washed with ether and triturated with warm alcohol gave the *hydrate* of (XVIII) in fawn-yellow hexagonal prisms (0·9 g.), m. p. 262° (decomp.) (Found: C, 57·3; H, 4·9. $C_{20}H_{16}O_9,H_2O$ requires C, 57·1; H, 4·8%). This compound gives a dark purple ferric reaction and forms a yellow solution in dilute sodium hydroxide solution. The *penta-acetate*, prepared by acetic anhydride–pyridine, formed prisms, m. p. 233° (decomp.), from dilute acetic acid (Found: C, 59·0; H, 4·5. $C_{30}H_{28}O_{14}$ requires C, 58·8; H, 4·6%).

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The Infrared Spectra of Some Esters, Nitriles, and Ester-nitriles.

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The unsaturated compound diethyl 1 : 2-dicyanoethylene-1 : 2-dicarboxylate was found to give a C:O band in a position close to that expected for a saturated ester but a C:N band in that expected for an unsaturated ester, and a very weak C:C band was also found. This behaviour has been explained on the basis of the electronic structure of the molecule by taking into account the appropriate inductive, mesomeric, and steric factors. Such an explanation has been made possible by a careful examination of these factors as they affect the C:O, C:N, and C:C frequencies in simple esters and nitriles and in related ester-nitriles.

IT has been shown (Felton, *J.*, 1955, 515) that oxidation of ethyl cyanoacetate by selenium dioxide yields diethyl 1 : 2-dicyanoethylene-1 : 2-dicarboxylate. Before this structure had been proved, the infrared spectrum of the compound was examined in order to decide between the two alternative structures then thought possible, *viz.*, the above and triethyl 1 : 2 : 3-tricyano*cyclo*propane-1 : 2 : 3-tricarboxylate. It was expected that these would readily be differentiated by comparison of the frequency of the ester-carbonyl band with that in the parent ethyl cyanoacetate, as a reduction of some 20 cm.$^{-1}$, due to the conjugation with the double bond, would be expected only for the former structure. This structure would also be expected to have a lower nitrile frequency and to exhibit an ethylene stretching frequency at about 1600 cm.$^{-1}$.

The oxidation product was found to give a carbonyl band at a position only slightly

lower than in ethyl cyanoacetate, *viz.*, at 1750 cm.$^{-1}$ compared with 1754 cm.$^{-1}$ (both in carbon tetrachloride solution). The nitrile band, however, was lowered from 2267 to 2229 cm.$^{-1}$ and a weak band at 1600 cm.$^{-1}$ was found (all in chloroform solution). Later, it was shown unequivocally that the oxidation product possessed the olefinic structure. The question then arose as to why the carbonyl frequency is higher than expected.

A series of related ester-nitriles and a number of simple esters and nitriles have been examined and the bands due to their carbonyl, nitrile, and olefinic groups, where present, have been measured in dilute solutions in carbon tetrachloride and chloroform. The values found are shown in the Tables. Previous measurements, to which reference is made in the

TABLE 1. *Frequencies* (ν *in cm.*$^{-1}$) *and intensities* (ε *in l. mole*$^{-1}$ *cm.*$^{-1}$) *for bands due to carbonyl and olefinic groups in esters.*

	C:O band frequencies:		C:C band in $CHCl_3$	
	in CCl_4	in $CHCl_3$	ν	ε
1. Ethyl acetate	1744	1733	—	—
2. Ethyl propionate	1740	1728	—	—
3. Diethyl malonate	1740 1757	1731 1747	—	—
4. Diethyl succinate	1740	1732	—	—
5. Tetraethyl ethanetetracarboxylate	1742 1751	1737 1746	—	—
6. Ethyl crotonate	1724	1712	1662	120
7. Ethyl α-methylacrylate	1721	1712	1638	81
8. Ethyl 3-methylbut-2-enoate	1720	1705	1654	170
9. Diethyl *iso*propylidenemalonate	1726	1719	1640	115
10. Diethyl fumarate	1727	1719	1647	95
11. Diethyl maleate	1734	1724	1646	95
12. Diethyl mesaconate	1725	1716	1649	110
13. Diethyl citraconate	1732	1723	1653	160
14. Tetraethyl ethylenetetracarboxylate	1739 1750	1737 1750	1651	35

TABLE 2. *Frequencies and intensities for the bands due to nitrile and olefinic groups in nitriles.* (ν_{weak} refers to the frequencies of bands accompanying the main C:N band with less than 10% of its intensity. ν_{Ar} and ε_{Ar} refer to bands arising from the presence of an aromatic structure.)

	C:N bands in $CHCl_3$			C:C bands in $CHCl_3$			
	ν	ε	ν_{weak}	ν	ε	ν_{Ar}	ε_{Ar}
15. Acetonitrile	2292 2255	13 32	—	—	—	—	—
16. Butyronitrile	2253	34	2293	—	—	—	—
17. Malonodinitrile	2273	7	2292	—	—	—	—
18. Succinodinitrile	2256	27	2275	—	—	—	—
19. Acrylonitrile	2231	38	2277	1647 1610	2·7 3·4	—	—
20. Crotononitrile	2228	81	—	1638	38	—	—
21. α-Methylacrylonitrile	2229	42	2210	1626	18	—	—
22. 3-Methylbut-2-enonitrile	2221	150	—	1637	32	—	—
23. (1-Ethylpropylidene)malonodinitrile	2234	110	—	1591	100	—	—
24. Benzylidenemalonodinitrile	2232	140	—	1594	180	1572	120
25. 1-Phenylethylidenemalonodinitrile	2230	93	—	1587	92	1568	100
26. Fumarodinitrile	2240	14	2260 2229	1612	3	—	—
27. Maleidinitrile	2251 2231	5·8 5·4	—	1630 1599	1·3 1·8	—	—
28. Mesaconodinitrile	2236	34	2226	1637 1616	10 11	—	—
29. Dimethylfumarodinitrile	2231	70	—	1645 1615	7 15	—	—
30. Dimethylmaleidinitrile	2224	51	—	1614	11	—	—
31. 3 : 4 : 5 : 6-Tetrahydro-*o*-phthalodinitrile	2227	61	—	1616	9	—	—
32. Phenylfumarodinitrile	2234 2223	20 24	—	1592	39	1570	42
33. Phenylmaleidinitrile	2225	62	2234	1590	51	1574	59
34. Methylphenylfumarodinitrile	2229	57	2219	1597	8	1576	9
35. Methylphenylmaleidinitrile	2226	57	—	1593	10	1577	10
36. Diphenylfumarodinitrile	2224	62	—	1619	10	1582	10

TABLE 3. *Frequencies and intensities for the bands due to carbonyl, nitrile, and olefinic groups in ester-nitriles.*

	C:O band frequencies:		C:N band in $CHCl_3$		C:C band in $CHCl_3$	
	in CCl_4	in $CHCl_3$	ν	ε	ν	ε
37. Ethyl cyanoacetate	1754	1751	2267	14	—	—
38. Diethyl 1 : 2-dicyanoethane-1 : 2-dicarboxylate	1755	1754	2259	13	—	—
39. Triethyl 1 : 2 : 3-tricyanocyclopropane-1 : 2 : 3-tricarboxylate	1765	1765	2260	10	—	—
40. Ethyl 2-cyanopent-2-enoate ...	1737	1732	2233	43	1602	132
41. Ethyl 2-cyano-3-ethylpent-2-enoate	1732	1727	2224	65	1629	123
42. Ethyl *trans*-β-cyanocrotonate	1728	1723	2228	28	1637	92
43. Ethyl *cis*-β-cyanocrotonate ...	1738 1725 (sh)	1728	2229	17	1642	80
44. Diethyl *trans*(?)-1 : 2-dicyanoethylene-1 : 2-dicarboxylate	1750	1747	2229	10	1600	6

Discussion, have been made on the simpler compounds, but these have not always been on dilute solutions. Only under the latter conditions can spectral changes due to causes other than structure be eliminated, so all values used have been determined in this work.

EXPERIMENTAL

Materials.—Ethyl acetate and propionate, diethyl malonate and succinate, ethyl α-methylacrylate and cyanoacetate and aceto- and butyro-nitrile, malono- and succino-dinitrile, and acrylo- and α-methylacrylo-nitrile were commercial samples, redistilled when required. Tetraethyl ethanetetracarboxylate, m. p. 76·5—77·5° (corr.), was prepared according to Mann and Saunders (" Practical Organic Chemistry," Longmans Green and Co., London, 1938, p. 190), and tetraethyl ethylenetetracarboxylate, m. p. 55·5—56·5° (corr.), according to Corson and Benson (*Org. Synth.*, Coll. Vol. II, p. 273). Diethyl *iso*propylidenemalonate, b. p. 118—120°/16 mm., n_D^{25} 1·4475, was prepared by Cope and Hancock's method (*J. Amer. Chem. Soc.*, 1938, **60**, 2645). Ethyl 3-dimethylbut-2-enoate, b. p. 60°/20 mm., n_D^{20} 1·4368, diethyl fumarate, b. p. 114—116°/15 mm., and diethyl maleate, b. p. 110—112°/16 mm., were obtained from the corresponding acids by azeotropic esterification, and diethyl citraconate, b. p. 114°/12 mm., $n_D^{20\cdot5}$ 1·4439, and diethyl mesaconate, b. p. 110°/16 mm., $n_D^{19\cdot5}$ 1·4484, were prepared according to Jeffery and Vogel (*J.*, 1948, 658).

3-Methylbut-2-enonitrile, b. p. 138—142°, $n_D^{21\cdot5}$ 1·4320, was prepared by distilling *iso*butyraldehyde cyanohydrin (Ultée, *Rec. Trav. chim.*, 1909, **28**, 7) over phosphoric oxide at atmospheric pressure (De Laet, *Bull. Soc. chim. belg.*, 1929, **38**, 163). (1-Ethylpropylidene)malonodinitrile, b. p. 114—115°/15 mm., n_D^{26} 1·4689, was prepared according to Cope and Hoyle (*J. Amer. Chem. Soc.*, 1941, **63**, 733), benzylidenemalonodinitrile, m. p. 86° (corr.), according to Corson and Stoughton (*ibid.*, 1928, **50**, 2825), and 1-phenylethylidenemalonodinitrile, m. p. 92·5—93·5° (corr.), according to Mowry (*ibid.*, 1943, **65**, 991). Fumarodinitrile, m. p. 97·5—98·5° (corr.), was obtained following the procedure of Mowry and Butler (*Org. Synth.*, 1950, **30**, 46), and maleidinitrile, m. p. 30—31° (corr.), following that of Linstead and Whalley (*J.*, 1952, 4839).

Ethyl 2-cyanopent-2-enoate, b. p. 115—120° (bath)/16 mm., was prepared by esterification of the acid (von Auwers, *Ber.*, 1923, **56**, 1172), and ethyl 2-cyano-3-ethylpent-2-enoate by Cope and Hancock's procedure (*Org. Synth.*, 1945, **25**, 46). Ethyl *cis*- (b. p. 116—118°/20 mm., n_D^{21} 1·4530) and *trans*-β-cyanocrotonate (b. p. 93—95°/20 mm., n_D^{21} 1·4508) were prepared according to Mowry and Rossow (*J. Amer. Chem. Soc.*, 1945, **67**, 926). The infrared spectrum of the *cis*-isomer gave an unexpected shoulder on the low-frequency side of the ester-carbonyl band, but this was not due to contamination with the *trans*-isomer. Through the courtesy of Dr. Mowry (Monsanto Chemical Co., St. Louis, Mo., U.S.A.) the original sample of the *cis*-isomer was obtained and its infrared spectrum was identical in all respects with that of the above sample.

The preparation of diethyl *trans*(?)-1 : 2-dicyanoethylene-1 : 2-dicarboxylate and of triethyl 1 : 2 : 3-tricyano*cyclo*propane-1 : 2 : 3-tricarboxylate has already been described (Felton, *J.*, 1955, 515 *).

Diethyl αβ-Dicyanosuccinate.—Diethyl 1 : 2-dicyanoethylene-1 : 2-dicarboxylate (2·2 g.) in ethanol (200 ml.) was shaken at room pressure and temperature with hydrogen and Adams's platinic oxide catalyst. After the uptake of 1 mol. of hydrogen, the catalyst was removed, the

* On line 20 of *J.*, 1955, 516, the temperature should read 120°.

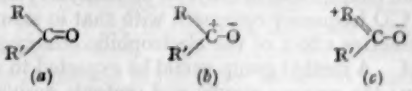
solvent evaporated, and the residue distilled to yield the *succinate*, b. p. 190—200° (bath)/10 mm. (Found : C, 53·9; H, 5·15; N, 12·8. $C_{10}H_{12}O_4N_2$ requires C, 53·6; H, 5·4; N, 12·5%).

Samples of crotononitrile, mesacono-, dimethylfumaro-, phenyl-malei- and -fumaro-, and methylphenyl-malei- and -fumaro-dinitrile (Beech and Piggott, *J.*, 1955, 423) and diphenylfumarodinitrile (Timmons and Wallwork, *Chem. and Ind.*, 1955, 62) were obtained from Imperial Chemical Industries Limited, Dyestuffs Division, through the great courtesy of Dr. M. A. T. Rogers; Drs. J. A. Elvidge and M. Whalley (Imperial College of Science and Technology, London, S.W.7) kindly provided samples of dimethylmaleidinitrile and 3 : 4 : 5 : 6-tetrahydro-*o*-phthalodinitrile.

Infrared Spectra.—The spectra were measured on a Perkin–Elmer Model 112 spectrometer. A rock-salt prism was used for the measurement of the carbonyl and olefinic bands (6μ) and one of lithium fluoride for the nitrile bands (4·5μ). The instrument was kept at a carefully controlled temperature, and the calibration checked repeatedly; as a result, the error in frequency in both regions cannot be more than ±2 cm.$^{-1}$, and duplicate measurements all agreed to within 1 cm.$^{-1}$. Solutions were measured in a 1 mm. cell and the intensities are quoted as approximate extinction coefficients (± about 10%) at the band maximum in l. mole^{-1} cm.$^{-1}$.

Discussion

It is well known that the frequency of a band due to the stretching of a multiple bond is dependent on the electronic structure around this bond, and in particular on its bond order. Thus, for carbonyl compounds the frequency due to this group has been considered (Hartwell, Richards, and Thompson, *J.*, 1948, 1436) in relation to the actual resonance



hybrid made up of the three forms (*a*)—(*c*). The relative importance of these forms will depend on the nature of the group R (and R'), and this may be considered in relation to the electronic shifts it produces by reason of its inductive or mesomeric effect. In addition, it is necessary, when conjugation between two unsaturated groups can occur, to take into account possible steric factors. If the necessary spatial arrangements do not allow a coplanar structure for two multiple bonds on either side of a single bond, the two π-orbitals will no longer be able to overlap to the fullest extent and conjugation will be either reduced or eliminated entirely. Conjugation can also be affected by changes in bond angles induced by steric repulsion between two similarly charged polar groups in close proximity, but then an increase or a decrease in conjugation can occur.

Previous applications of such considerations have been made mainly in cases where a single effect is operative and do not cover many of the frequency values now reported, especially those of the polyfunctional compounds. Two main effects have been discussed in the case of esters: first, the inductive effect of an electrophilic group on the α-carbon atom, which reduces the contributions to the resonance hybrid of the ionic forms (*b*) and (*c*) and thus increases the C:O frequency, has been observed for α-halogeno- and α-cyano-acetates (Hartwell, Richards, and Thompson, *loc. cit.*; Hampton and Newell, *Analyt. Chem.*, 1949, **21**, 914; Rasmussen and Brattain, *J. Amer. Chem. Soc.*, 1949, **71**, 1073); and, secondly, the mesomeric effect of an unsaturated group leads to increased contributions of the ionic forms owing to their stabilisation by the greater separation of charge, and the consequent reduction in C:O frequency has been observed in both olefinic and aromatic esters (Hartwell, Richards, and Thompson; Hampton and Newell; Ramussen and Brattain, *locc. cit.*). In the case of the nitriles, the C:N bands of a large number, including compounds 15—21, 26, and 29 in the Tables, have been measured by Kitson and Griffith (*Analyt. Chem.*, 1952, **24**, 334) and the reduction in frequency consequent on conjugation with an unsaturated centre has been pointed out.

These explanations have been made to cover the larger shifts in the positions of the C:O and C:N bands, but there is no doubt that even small shifts, when obtained for solutions in the same solvent, are significant and can be correlated with structure on the same basis,

as has been shown for keto-steroids and steroid esters (Jones, Humphries, and Dobriner, *J. Amer. Chem. Soc.*, 1950, **72**, 956). Thus, the slight reduction of C:O frequency in ethyl propionate (2) compared with ethyl acetate (1) is in line with the greater electron-repelling effect of methyl than of hydrogen; the strongly electron-attracting nitrile group produces a shift, which is both larger and in the opposite direction, of 10 cm.$^{-1}$ between ethyl acetate (1) and ethyl cyanoacetate (37). A similar increase would be expected with diethyl malonate (3), but splitting of the C:O band precludes its observation, although the mean position of the two components is certainly above that of the band in ethyl acetate. A similar situation arises in tetraethyl ethanetetracarboxylate (5). The splitting may be due to symmetric and antisymmetric coupling of the two C:O stretching vibrations or to their resonance coupling with an overtone. Analogous effects are observed for the nitrile frequency; its value in acetonitrile (15) is decreased slightly in going to butyronitrile (16), but increased by 12 cm.$^{-1}$ in ethyl cyanoacetate and 18 cm.$^{-1}$ in malonodinitrile (17). The difference in these last two figures agrees with the known stronger electron-attracting power of the nitrile group; this may also explain why the insulating effect of the extra methylene group is sufficient to prevent interaction of the two ester groups in diethyl succinate (4) while the C:N frequency in succinodinitrile (18) is slightly increased.

The unsaturated crotonic compounds show reduction in the respective frequencies compared with the saturated compounds of 20 cm.$^{-1}$ for the ester (6) and 27 cm.$^{-1}$ for the nitrile (20). This is due to the electromeric effect already described. An inductive effect can be transmitted by the olefinic bond so that the groups attached to the β-carbon atom have much the same effect as those on the α-atom. Rasmussen and Brattain (*loc. cit.*) pointed out that the small conjugation in ethyl ββ-diethoxyacrylate as shown by the smallness of the reduction in C:O frequency compared with that in saturated esters must be due to opposition by the inductive effect of the electrophilic ethoxy-groups to the mesomeric effect of the olefinic bond. A methyl group would be expected to show a smaller effect and in the opposite direction; the various acrylic and crotonic derivatives (6—8 and 19—22) show this effect by a lowering of the C:O or C:N frequency with methyl substitution. The electromeric effect also reduces the double-bond character of the C:C link itself, giving rise to a band at a lower position. The actual reduction in comparison to the hydrocarbon varies, but in each case it is about 18 cm.$^{-1}$ lower in the nitrile than in the corresponding ester, as would be expected from the higher electron-attracting power of the nitrile group.

Compounds in which more than one ester or nitrile group is attached to an olefinic bond must now be considered; it is this class about which little is known and which includes the ester-nitrile whose olefinic structure seemed to be contra-indicated by its C:O frequency.

First, let us take the case where two of these groups are on the same carbon atom. Then either may be conjugated with the C:C double bond, but not together because they are cross-conjugated. The fact that both are electron-attracting groups implies that the electron drift across the C:C bond must be shared between the two groups, so that although a greater drift would be expected to be caused by two groups than by one, the effect on individual substituent groups should be smaller. In accordance with this expectation, diethyl *iso*propylidenemalonate (9) has a lower C:C frequency by 14 cm.$^{-1}$, but a higher C:O frequency by 6 cm.$^{-1}$, than ethyl 3-methylbut-2-enoate (8). Similarly (1-ethylpropylidene)-malonodinitrile (23) has a lower C:C frequency by 46 cm.$^{-1}$ but a higher C:N frequency by 13 cm.$^{-1}$ than 3-methylbut-2-enonitrile (22); the frequencies observed for benzylidene-malonodinitrile (24) and its methyl derivative (25) are also in line with this effect. In the ester-nitriles, the resonance form with an ionic nitrile group must have a lower energy than that with an ionic ester group, because of the greater electron-attracting power of the former, and that form is therefore favoured. Consideration of ethyl 2-cyano-3-ethyl-pent-2-enoate (41) shows the competing effects of these two groups; compared with the diester (9) and the dinitrile (23), the C:O frequency is raised by 6 cm.$^{-1}$ and the C:N frequency is lowered by 10 cm.$^{-1}$, while the C:C frequency is intermediate between those of the unmixed compounds; compared with the monoester (8), the C:O frequency is raised by 12 cm.$^{-1}$, although still 22 cm.$^{-1}$ below that of the saturated ethyl cyanoacetate, while the C:N frequency is raised only 3 cm.$^{-1}$ compared with the mononitrile (22) and is 43 cm.$^{-1}$ below that in the saturated compound. Similarly, comparison of ethyl 2-cyanopent-2-enoate (40)

with its related monoester (6) and mononitrile (20) shows the C:O and C:N frequencies to be increased by 13 cm.$^{-1}$ and 5 cm.$^{-1}$ respectively. The low C:C frequency in these asymmetric disubstituted compounds has already been noted; this band is also characterised by a high intensity, which would be expected from the high polarity of the bond induced by the two electron-attracting groups' being on the same carbon atom and therefore reinforcing one another.

When two of these groups are attached to opposite ends of the ethylenic bond, their electron-attracting properties will tend to polarise that bond in opposite directions. The resonance hybrid will be such that the oxygen or the nitrogen atom will be negatively charged and both olefinic carbon atoms positively charged; the separation of charge inherent in the ionic form of each polar group is therefore effectively relayed only to the α-carbon atom of the olefinic link and not to the β-atom as in the unsaturated mono-ester or nitrile. A higher ester-carbonyl or nitrile frequency would therefore be expected, and this is found. Examination of the *trans*-diesters, diethyl fumarate (10) and mesaconate (12) shows an increase of about 5 cm.$^{-1}$ in the C:O frequency above that in the appropriate monoester, while the *trans*-dinitriles (26) and (28) are increased about 10 cm.$^{-1}$ in their C:N frequency; in the *trans*-β-cyanocrotonate (42) the effect on the carbonyl frequency is slightly greater and on the nitrile frequency slightly less, a result which would be expected from the greater electron-attracting power of the nitrile group. These shifts are all comparable with those found in the asymmetrically disubstituted compounds, but the two classes differ as regards the intensity of the band due to the C:C bond. Compared with that of the monosubstituted compounds, its polarity is increased in the asymmetrically disubstituted compounds, but decreased in the symmetric ones (to zero in the completely symmetric compounds) so that the intensity of the band associated with its stretching is respectively increased and reduced. This effect occurs in both esters and nitriles, but the reduction is particularly noticeable in the latter, doubtless because the electron density is lower than in the esters.

The situation with the *cis*-disubstituted compounds is complicated by steric factors. An assessment of their importance has been made from a consideration of atomic models. In the *cis*-diesters, there would be considerable steric hindrance did not a non-planar structure obtain. The resultant reduction in conjugation increases the C:O frequency: thus, the absorption in diethyl maleate (11) is at 1734 cm.$^{-1}$, compared with 1727 cm.$^{-1}$ in diethyl fumarate, and is only 6 cm.$^{-1}$ below that in the saturated diethyl succinate; diethyl citraconate (13) is similarly 7 cm.$^{-1}$ above diethyl mesaconate in its C:O frequency. This effect has already been noted in the higher C:O frequency of diallyl maleate than in diallyl fumarate (Hampton and Newell, *loc. cit.*). In the dinitriles, there is no steric hindrance but the two nitrile groups are close to one another and, both being negatively charged, can be expected to repel one another. This leads to a more linear structure, a feature which should increase the conjugation of the olefinic bond with the nitrile groups, and so decrease the frequency of their stretching vibration. Four isomeric pairs of nitriles (26–27, 29–30, 32–33, and 34–35) have been examined and the C:N frequency in the *cis*-isomer appears to be about 5 cm.$^{-1}$ lower than in the *trans*-isomer; unfortunately, the band is split in two cases, so that any shift is masked. The slightly higher C:N frequency of 3 : 4 : 5 : 6-tetrahydro-*o*-phthalodinitrile (31) than in dimethylmaleidinitrile (30) may be due to the ring's opposing any change in bond angle resulting from steric repulsion. In the case of ethyl *cis*-β-cyanocrotonate (43) steric repulsion between the two polar groups should again occur, but in this case is most easily accommodated by a rotation of the ester group to a non-planar configuration. In agreement with this, the C:O frequency is 10 cm.$^{-1}$ above that in the *trans*-compound while the C:N frequency is at about the same position.

In the tetrasubstituted compounds all the factors must be considered together. Thus, in tetraethyl ethylenetetracarboxylate (14), the four ester groups are all tending to attract electrons and therefore oppose one another; further, they can only be sterically accommodated in a non-planar configuration. The result should be for the electronic state of the ester groups to be similar to that in the saturated ethyl ethanetetracarboxylate; this is so, for the C:O absorption, double in both cases, is only slightly lower in the unsaturated compound. In the diethyl dicyanoethylenedicarboxylate (44), the four polar

groups are again in opposition; the ester groups are the weaker electron-attracting groups, and are, moreover, forced into non-planar configurations by steric repulsion from the nitrile groups so that the olefinic link must be conjugated mainly with the latter. The compound should therefore behave as unsaturated with respect to its nitrile groups, but saturated with respect to its ester groups. These considerations explain the high C:O frequency of 1750 cm.$^{-1}$, only 5 cm.$^{-1}$ lower than in the saturated ethane analogue (38), and the C:N frequency of 2229 cm.$^{-1}$ which is by contrast 30 cm.$^{-1}$ lower than in the ethane compound, and at about the expected position for an unsaturated nitrile. The low intensity of the C:C band is to be expected because the electronic distribution in the link is symmetrical and at a low level.

The conclusion to be drawn from these measurements and their interpretations is that great care should always be taken to allow for all possible effects when using infrared spectra in the elucidation of molecular structure. It has been shown that quite small effects, when cumulative, can lead to considerable shifts in characteristic frequencies in strongly polar molecules.

This investigation has been supported by grants to this Institute from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service. The authors are indebted to Drs. M. A. T. Rogers, D. T. Mowry, J. A. Elvidge, and M. Whalley for the generous gift of samples, and to Mr. J. M. Johnson for technical assistance with some of the preparations.

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Studies in the Steroid Group. Part LXVIII. Epidioxides derived from Lumisterol and Related Compounds.*

By Peter Bladon.

[Reprint Order No. 5929.]

The photochemical reaction of lumisteryl acetate with oxygen yields dehydrolumisteryl acetate, lumisteryl acetate β-epidioxide, dehydrolumisteryl acetate α- and β-epidioxides, and 3β-acetoxylumista-5 : 8(9) : 22-trien-7-one. The structure of the β-epidioxides follows from their rearrangement in alkaline solution to 8β-hydroxylumista-4 : 6-dien-3-ones.† The mechanism of this reaction is discussed. The 7-ketone is readily transformed into a phenol by the dienone–phenol rearrangement.

In several papers (Bladon, Clayton, Greenhalgh, Henbest, Jones, Lovell, Silverstone, Wood, and Woods, *J.*, 1952, 4883; Henbest, Jones, Wood, and Woods, *J.*, 1952, 4894; Clayton, Crawshaw, Henbest, Jones, Lovell, and Wood, *J.*, 1953, 2009; Clayton, Henbest, and Jones, *J.*, 1953, 2015; Bladon, Henbest, Jones, Lovell, and Woods, *J.*, 1954, 125), the use of dehydroergosterol and ergosterol epidioxides as intermediates in the synthesis of cortical hormones was described. As an extension to that work, this paper describes the analogous epidioxides from lumisterol (I; R = H) (the isomer of ergosterol having the $C_{(10)}$-methyl group in the α-configuration). The work also forms part of investigations of steroids having abnormal configurations at one or more of the angular positions, being carried out in these laboratories.

* Part LXVII, *J.*, 1954, 800.

† Compounds described in this paper having a 10α-methyl group are named as derivatives of lumistane. The configuration of atoms or groups at the asymmetric carbon atoms $C_{(8)}$ and $C_{(9)}$ is indicated in the name when it is known, but unless otherwise stated the hydrogen atom at $C_{(9)}$ has the α-configuration.

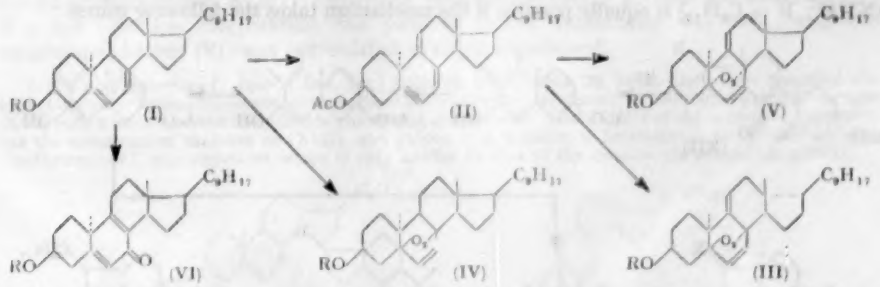
There is no literature record of the preparation of an epidioxide (peroxide) from lumisterol.* Accordingly the method used for preparing dehydroergosterol epidioxide (Bladon, Clayton, *et al.*, *loc. cit.*) and ergosterol peroxide (Clayton, Henbest, and Jones, *loc. cit.*) was used initially with lumisteryl acetate (I; R = Ac) as starting material. To avoid hydrolysis alkali was not added to the reaction mixture, but to minimise the effects of acid, which is thought to arise from oxidative splitting of the side-chain double bond, a small amount of pyridine was added.

Under these conditions oxygen was taken up readily at the temperature of refluxing ethanol, the reaction being complete in 16 hr. Although a fairly pure solid could be isolated by direct crystallisation, discrepancies in the optical rotation of samples pointed to its being impure, and by chromatography on alumina four pure substances were isolated.

The products in ease of elution were: (i) The known 9(11)-dehydrolumisteryl acetate (II). (ii) The epidioxides. Separation of these compounds was not clear-cut, and was followed by change in rotation. The two compounds isolated were (in order of elution): 3β-acetoxy-5β : 8β-epidioxylumista-6 : 9(11) : 22-triene (dehydrolumisteryl acetate β-epidioxide) (III; R = Ac) (obtained also directly from dehydrolumisteryl acetate, see below), and 3β-acetoxy-5β : 8β-epidioxylumista-6 : 22-diene (lumisteryl acetate β-epidioxide) (IV; R = Ac). Several other fractions were mixtures of these compounds and probably dehydrolumisteryl acetate α-epidioxide (V; R = Ac). The assignment of the configurations of the epidioxides is discussed later. (iii) 3β-Acetoxylumista-5 : 8(9) : 22-trien-7-one (VI; R = Ac), the structure being assigned on the following evidence.

The infrared spectrum showed the presence of an unsaturated ketone function, an acetyl group, and the Δ^{22} side-chain double bond. Analyses of the compound and of the corresponding hydroxy-derivative favour $C_{30}H_{44}O_3$ and $C_{28}H_{42}O_2$ respectively, indicating the presence of two double bands in the nucleus.

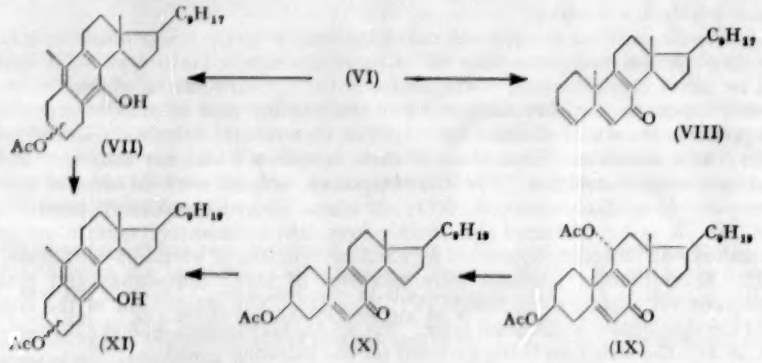
The ultraviolet spectrum ($\lambda_{max.}$ 246 mμ; ε 11,800) precludes an αβ–γδ unsaturated ketone system and suggests the cross-conjugated $\Delta^{5:8(9)}$-7-ketone. The ergosterol analogue of (VI) (Elks, Evans, Long, and Thomas, *J.*, 1954, 451; Elks, Evans, Oughton, and Thomas, *ibid.*, p. 463) has $\lambda_{max.}$ 245 mμ (ε 11,800). The other cross-conjugated system, a $\Delta^{4:7}$-6-ketone, is also a possibility, although the absorption would be expected to show a maximum



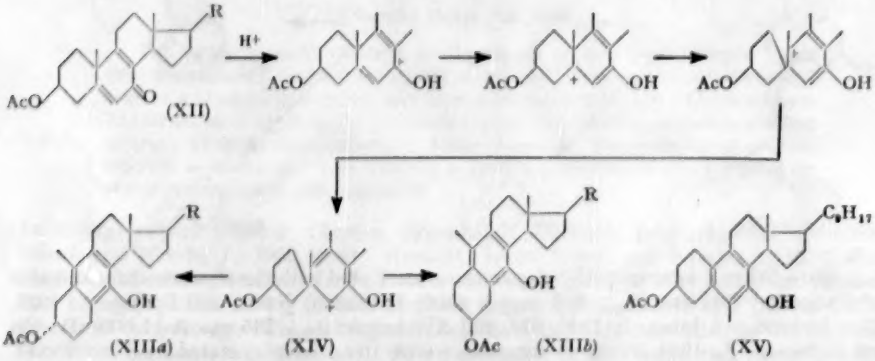
($\lambda_{max.}$ 240—241 mμ) intermediate between those associated with the separate chromophores [Δ^4-3β-acetoxy-6-ketone ($\lambda_{max.}$ 236 mμ; ε 6300) (Heilbron, Jones, and Spring, *J.*, 1937, 801; Jackson and Jones, *J.*, 1940, 659) and Δ^7-6-ketone ($\lambda_{max.}$ 245 mμ; ε 14,000) (Barton and Robinson, *J.*, 1954, 3045)] in accordance with the principles stated by Elks, Evans, Long, and Thomas (*loc. cit.*). This alternative is excluded by failure of treatment with activated zinc and acetic acid to cause elimination of the acetoxy-group, a reaction characteristic of γ-acetoxy- and γ-hydroxy-αβ-unsaturated ketones (Amendolla, Rosenkranz, and Sondheimer, *J.*, 1954, 1226; Fieser, *J. Amer. Chem. Soc.*, 1953, **75**, 4377; Barton and Laws, *J.*, 1954, 52). Instead these reagents caused rearrangement to a phenol (VII),

* Fieser and Fieser, "Natural Products related to Phenanthrene," Reinhold Publishing Corporation, New York, 3rd Edn., 1949, p. 173, and Shoppee, in Rodd, "Chemistry of Carbon Compounds," Elsevier Publishing Company, Amsterdam, 1954, Vol. II*B*, p. 851, mention "a peroxide of lumisterol"; these are, however, misprints for "an epoxide."

which proves the presence of the $\Delta^{5:8(9)}$-7-ketone system. The dienone–phenol rearrangement is well known among $\Delta^{1:4}$-3-ketosteroids (Inhoffen and Stoeck, *Annalen*, 1949, **563**, 127; Inhoffen and Becker, *Chem. Ber.*, 1953, **86**, 116; Wilds and Djerassi, *J. Amer. Chem. Soc.*, 1946, **68**, 1712, 2125; Djerassi and Scholz, *ibid.*, 1947, **69**, 2404; 1948, **70**, 1911; *J. Org. Chem.*, 1948, **13**, 697; Djerassi, *ibid.*, p. 848), but hitherto only two examples have



involved ring B dienones. Barton and Thomas (*J.*, 1953, 1842) describe the rearrangement of 7-oxolanosta-5 : 8-dien-3β-yl acetate with zinc and acetic acid (silver nitrate not added), but do not assign a structure to the phenol formed ($\lambda_{max.}$ 287 mμ; ε 3500 in neutral solution and $\lambda_{max.}$ 302 mμ; ε 3500 in alkaline solution), and Kyosuke Tsuda, Ko Arima, and Ryoichi Hayatsu (*J. Amer. Chem. Soc.*, 1954, **76**, 2933) describe the rearrangement of 7-oxocholesta-5 : 8-dien-3β-yl acetate (XII; R = C_8H_{17}) with sulphuric acid in acetic anhydride, and the subsequent dehydrogenation of the phenol to a mixture of anthracene derivatives. On the basis of this evidence they assign the phenol the structure (XIII*a*; R = C_8H_{17}) with the acetoxy-group in position 3 *. However, the 2-acetoxy-structure (XIII*b*; R = C_8H_{17}) is equally possible if the mechanism takes the following course:



It is impossible on the available evidence to decide in which direction the asymmetrical *spiro*-intermediate (XIV) will rearrange.

It is not certain that the rearrangement of the lumisterol derivative takes a similar course and yields an octahydroanthracene derivative (VII; OAc group in position 2 or position 3) rather than the alternative course involving migration of the angular methyl group to a 6-methyl-19-*nor*-steroid phenol (XV), because in the present case it has been impossible to effect the rearrangement by the conventional reagents.

It is implicit in this mechanism that the asymmetry at $C_{(10)}$ is lost in the reaction, and

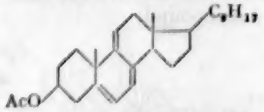
so it should be possible to obtain the same compounds from the lumisterol and the ergosterol series. This has been achieved. Treatment of 3β : 11α-diacetoxyergosta-5 : 8(9)-dien-7-one (IX; *J.*, 1953, 2916), with zinc and acetic acid in the presence of a *small* amount of silver nitrate, resulted in formation of 3β-acetoxyergosta-5 : 8(9)-dien-7-one (X). With a larger amount of silver nitrate, rearrangement to the phenol (XI) occurred. This same phenol was obtained on hydrogenating the side-chain double bond in the phenol (VII) obtained in the lumisterol series.*

Mild hydrolysis of the acetoxylumistatrienone (VI; R = Ac) yields the corresponding 3-hydroxy-compound (VI; R = H). However, under more vigorous conditions as would be expected for a αβ-unsaturated δ-hydroxy-ketone [cf. the formation of cholesta-3 : 5-dien-7-one from 7-ketocholesteryl acetate (Mauthner and Suida, *Monatsh.*, 1896, **17**, 579)] dehydration ensues with formation of lumista-3 : 5 : 8(9) : 22-tetraen-7-one (VIII), the light absorption of which ($\lambda_{max.}$ 272—273 mμ; ε 13,800) agrees with that of the corresponding ergosterol analogue ($\lambda_{max.}$ 272 mμ; ε 14,600) (Elks, Evans, Oughton, and Thomas, *loc. cit.*).

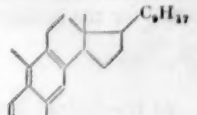
The complexity of the products from the photo-oxygenation prompted study of the reaction at lower temperatures. The temperature of refluxing ethanol was used in preparing ergosterol and dehydroergosterol epidioxides largely on account of the low solubilities in cold alcohol. However successful preparations were carried out in the cold (private communication from Dr. R. M. Evans of Glaxo Laboratories, Greenford, Middlesex). Because of the greater solubility of lumisterol derivatives, the high temperature was not essential. An apparatus similar to that described by Barton and Laws (*J.*, 1954, 52) was used, with eosin as sensitising dye. Lumisteryl acetate then gave three products: dehydrolumisteryl acetate (II), lumisteryl acetate β-epidioxide (IV; R = Ac), and 3β-acetoxylumista-5 : 8(9) : 22-trien-7-one (VI). Careful chromatography of the products failed to reveal the presence of any other epidioxide.

Dehydrolumisteryl acetate gave under both high- and low-temperature conditions, the same mixture of two epidioxides, the most easily eluted from the chromatogram column being identical with the material (III; R = Ac) isolated in the high-temperature photo-oxygenation of lumisteryl acetate. The second compound is the isomeric 3β-acetoxy-5α : 8α-epidioxylumista-6 : 9(11) : 22-triene (dehydrolumisteryl acetate α-epidioxide) (V; R = Ac). At low temperature the yield of mixed epidioxides was 83%, and the unsaturated ketone (VI) was not isolated in either experiment.

* Nes and Mosettig (*J. Amer. Chem. Soc.*, 1953, **75**, 2787; 1954, **76**, 3182, 3186) have described the formation of a hydroanthracene hydrocarbon derivative by treatment of dehydroergosteryl acetate (XVI) with a small amount of hydrogen chloride in chloroform. One (XVII) of the suggested structures has the same carbon skeleton as (XIII), and indeed it is possible to formulate a mechanism for this "anthrasteroid" rearrangement which is very similar to that of the dienone–phenol rearrangement.

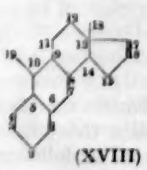


(XVI)

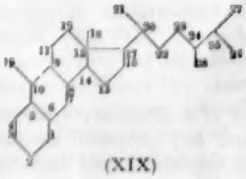


(XVII)

These authors term the parent saturated ring system (XVIII) "anthrastane" and the system with an ergostane side chain (XIX) "ergosanthrastane."



(XVIII)



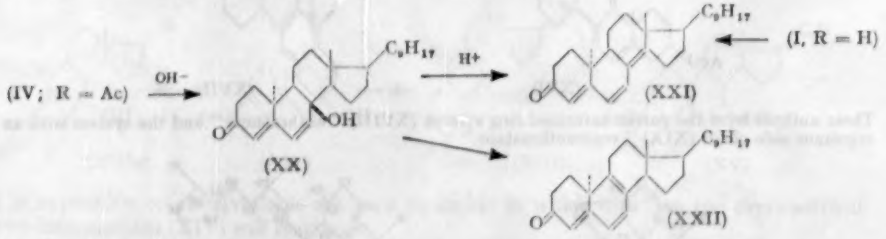
(XIX)

The numbering system used follows the suggestion of Inhoffen and Brückner (*Fortschr. Chem. org. Naturstoffe*, 1954, **11**, 83). Thus the product of the dienone–phenol arrangement of the lumisterol derivative is 3α- (or 2β-)-acetoxyanthraergosta-5 : 7 : 9 : 22-tetraen-7-ol.

Failure to isolate lumisteryl acetate α-epidioxide from the photochemical oxidation of lumisteryl acetate, while two epidioxides are obtained from dehydrolumisteryl acetate, suggests that this α-epidioxide is unstable. Furthermore, since in the cold, lumisteryl acetate does not give the dehydrolumisteryl acetate epidioxides, but only when hot, it may be supposed that initially lumisteryl acetate α-epidioxide is formed (together with the β-epidioxide), and at high temperature, or in working up, this breaks down to dehydrolumisteryl acetate and possibly the ketone (VI).

Ergosterol and dehydroergosterol epidioxides are stable in alkaline solution (Clayton, Henbest, and Jones, *loc. cit.*), as expected with compounds in which the epidioxide bridge joins two tertiary carbon atoms. It was somewhat surprising, therefore, that hydrolysis of lumisteryl acetate β-epidioxide yielded not the 3-hydroxy-compound but a compound $C_{28}H_{42}O_2$. The infrared spectrum shows the presence of a hydroxyl group (which is not acetylated by acetic anhydride and pyridine at room temperature, and is therefore most likely tertiary) and an unsaturated ketone group, and the absence of an acetyl group. The ultraviolet spectrum ($\lambda_{max.}$ 282—285 mμ; ε 26,000) corresponds to either a $\Delta^{3:5}$-7-ketone [Greenhalgh, Henbest, and Jones, *J.*, 1952, 2375; Jackson and Jones, *J.*, 1940, 659 ($\lambda_{max.}$ 277—280 mμ; ε 24,000—28,000)] or a $\Delta^{4:6}$-3-ketone [Wilds and Djerassi, *J. Amer. Chem. Soc.*, 1946, **68**, 1712; Prelog, Ruzicka, and Stein, *Helv. Chim. Acta*, 1943, **26**, 2237; Antonucci, Bernstein, Giancola, and Sax, *J. Org. Chem.*, 1951, **16**, 1453 ($\lambda_{max.}$ 284 mμ; ε 28,000)]. The second alternative is favoured because the large negative rotation ($[\alpha]_D$ −377°) corresponds to that of cholesta-3 : 5-dien-7-one ($[\alpha]_D$ −300°; Greenhalgh, Henbest, and Jones, *loc. cit.*) rather than that of the isomeric cholesta-4 : 6-dien-3-one ($[\alpha]_D$ +32°; *idem, ibid.*). The α-configuration of the $C_{(10)}$ methyl group in lumista-4 : 6-dien-3-one and lumista-3 : 5-dien-7-one places these compounds in the same stereochemical groups as cholesta-3 : 5-dien-7-one and cholesta-4 : 6-dien-3-one, respectively (cf. Stokes and Bergmann, *J. Org. Chem.*, 1952, **17**, 1194). The alkaline hydrolysis product is therefore assigned the structure 8β-hydroxylumista-4 : 6 : 22-trien-3-one (XX).

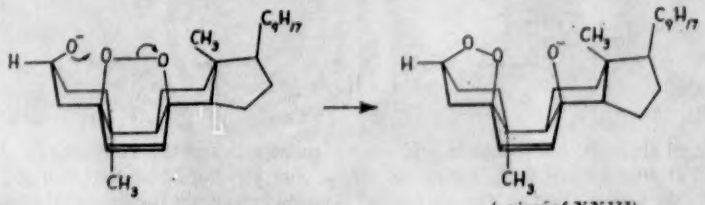
This is proved (particularly with respect to the position of the hydroxyl group and the retention of the normal lumisterol skeleton) by the *trans*-elimination of water in the presence of mineral acid to yield the lumista-4 : 6 : 8(14) : 22-tetraen-3-one (XXI) ($\lambda_{max.}$ 285; ε 8000 and 350—358 mμ; ε 25,000) which was also obtained directly by treatment of lumisterol (I; R = H) with *p*-benzoquinone and aluminium *tert.*-butoxide (cf. Wettstein, *Helv. Chim. Acta*, 1940, **23**, 388; Swiss P. 236,309; Dauben, Eastham, Micheli, Takemura, Mandell, and Chemerda, *J. Amer. Chem. Soc.*, 1953, **75**, 3255). Elks (*J.*, 1954, 468) records $\lambda_{max.}$ 237 (ε 4700), 282 (ε 7100), and 350 mμ (ε 27,100) for the corresponding ergosterol compound similarly prepared. The other direction of *trans*-dehydration to yield lumista-4 : 6 : 8(9) : 22-tetraen-3-one (XXII) ($\lambda_{max.}$ 244; ε 17,900 and 393 mμ; ε 11,000) occurred with refluxing acetic anhydride and pyridine. Elks (*loc. cit.*) records $\lambda_{max.}$ 244·5 (ε 16,700) and 390 mμ (ε 9300) for the analogous ergosterol compound.



The instability of a ditertiary epidioxide system in alkaline solution has not hitherto been reported, and any proposed mechanism must explain the difference between the behaviour of the ergosterol and lumisterol compounds. The following explanation is tentatively advanced.

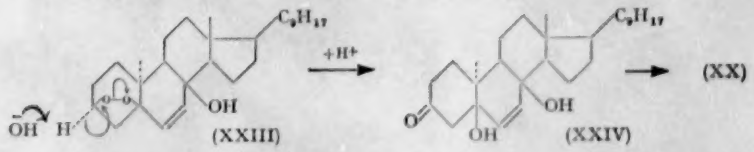
Molecular models of lumisterol α- and β-epidioxides reveal that only in the β-isomer are the two oxygen atoms ($C_{(3)}$–OH and $C_{(5)}$–O) close together, both being axial with respect

to ring A (ring B must of necessity be in a boat form). If it is supposed that the first step is the formation of an anion at $C_{(3)}$, then rearrangement can readily occur to give a hypothetical intermediate having a hydroxyl at $C_{(3)}$ and a $C_{(3)}$–$C_{(5)}$ epidioxide bridge (XXIII) *. (The three oxygen atoms $C_{(3)}$–OH, $C_{(5)}$–O, and $C_{(8)}$–O are nearly collinear.) By analogy



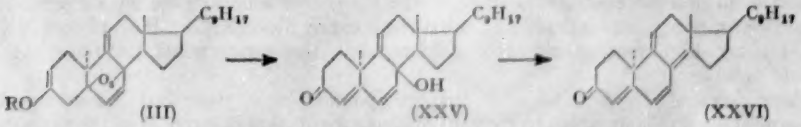
(anion of XXIII)

with other secondary–tertiary epidioxides (Skau and Bergmann, *J. Org. Chem.*, 1938, **3**, 166; Conca and Bergmann, *J. Org. Chem.*, 1953, **18**, 1104; Bergmann and Mclean, *Chem. Rev.*, 1941, **28**, 367; Laubach, Schreiber, Agnello, Lightfoot, and Brunings, *J. Amer. Chem. Soc.*, 1953, **75**, 1514; cf. Kornblum and de la Mare, *J. Amer. Chem. Soc.*, 1951, **73**, 880) the epidioxide (XXIII) would be expected to be attacked by hydroxyl or alkoxyl anions:



the intermediate 5-hydroxy-3-ketone (XXIV) would be dehydrated by alkali to yield the 8-hydroxy-dien-3-one (XX).

Such a series of reactions would be impossible in the ergosterol series, where the 3β-equatorial hydroxyl group is too far removed from the epidioxide bridge, and also with (the unknown) lumisterol α-epidioxide, where the epidioxide bridge is on the opposite side of the molecule to the hydroxyl group. The correctness of this scheme was shown since, of the two isomeric dehydrolumisteryl acetate epidioxides, only one isomer, which is hence established as (III; R = Ac), underwent rearrangement; the intermediate 8-hydroxy-compound (XXV) was very unstable; with traces of acid it readily gave lumista-4 : 6 : 8(14) : 9(11) : 22-pentaen-3-one (XXVI).

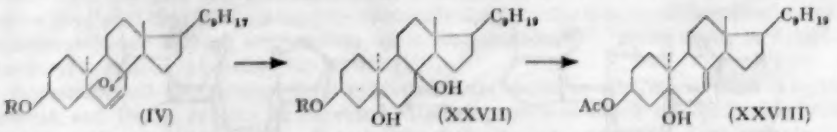


In contrast, the other epidioxide (V; R = Ac) was hydrolysed by alkali to 5α : 8α-epidioxy-3β-hydroxylumista-6 : 9(11) : 22-triene (V; R = H). This compound was however unstable to crystallisation; the nature of the decomposition products was not determined.

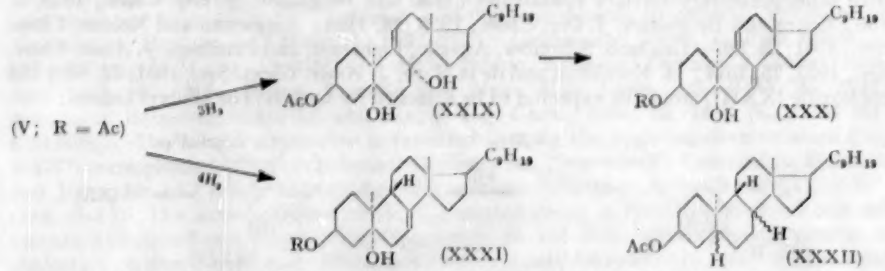
Hydrogenation of lumisteryl acetate β-epidioxide in the presence of Adams's catalyst readily afforded 3β-acetoxylumistane-5β : 8β-diol (XXVII; R = Ac) which differs markedly from the corresponding ergosterol analogue (Clayton, Henbest, and Jones, *loc. cit.*). The infrared spectrum in carbon disulphide shows two sharp hydroxyl peaks (at 3565 and 3435 cm.$^{-1}$) which do not change in relative intensity on change of concentration. This shows that there is little intramolecular and no intermolecular hydrogen bonding between the groups. That the hydroxyl groups are extremely hindered

* This rearrangement is in effect an internal S_Ni reaction with attack on an oxygen instead of a carbon atom.

is shown by the ease of elution of the compound with benzene from alumina. The compound is more stable towards acidic reagents than the ergosterol analogue; it was unchanged by treatment with refluxing acetic acid in acetone whereas under these conditions, the ergosterol compound gives a 5 : 8-epoxide. Phosphoryl chloride in



pyridine, and alcoholic hydrochloric acid were without effect of this compound. However, acetic acid at 100° caused dehydration, to give a poor yield of 3β-acetoxylumist-7-en-5β-ol (XXVIII) (the formulation of this compound is based largely on the doubtful analogy with the ergosterol series).



Similar hydrogenation of dehydrolumisteryl acetate α-epidioxide (V; R = Ac) with 3 mols. of hydrogen gave a syrup, presumably the diol (XXIX), which was readily dehydrated to 3β-acetoxylumista-7 : 9(11)-dien-5α-ol (XXX; R = Ac). With 4 mols. of hydrogen the major product was 3β-acetoxy-9β-(?)-lumist-7-en-5α-ol (XXXI; R = Ac). The structure of this compound is in some doubt however; the 9β-structure is adduced from the known direction of hydrogen addition to dehydrolumisteryl acetate to yield hexahydropyrocalciferol acetate (XXXII) (Dimroth, *Ber.*, 1936, **69**, 1123), in which the hydrogen at C_9 must be β-orientated consequent upon its formation from pyrocalciferol *via* the dihydro-compound (Busse, *Z. physiol. Chem.*, 1933, **214**, 211). On the other hand the double bond may be in the 8 : 9-position. The compounds derived from dehydrolumisteryl acetate α-epidioxide by hydrogenation (XXX and XXXI; R = Ac) have properties in marked contrast to those of the lumisteryl acetate β-epidioxide series; the hydroxy-groups are not hindered and the corresponding diols (XXX; R = H, and XXXI; R = H) are high-melting insoluble compounds; the series generally resembles the ergosterol series.

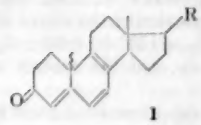
Stereochemical Implications.—Several compounds now described have ergosterol analogues and it is instructive to compare molecular-rotation differences in the pairs in the lumi- and ergo-sterol series differing by inversion of configuration at $C_{(10)}$ (cf. Fieser and Fieser, *op. cit.*, p. 212). Table 1 lists the molecular rotations for such pairs of compounds, together with the difference between them and the average value for the pair.

It is seen at once that there is no constant difference in $[M]_D$ for a change of configuration at $C_{(10)}$. The reason for this is probably that all the compounds listed have powerful chromophores, and the rotations are therefore complicated by optical exaltation (cf. Karrer and Kasse, *Helv. Chim. Acta*, 1919, **2**, 436). On the other hand, these compounds are those with which comparisons are best made, for pairs of saturated derivatives of lumisterol and ergosterol would not give reliable values, because such lumisterol derivatives must frequently necessarily have one of their rings in a boat form.

The average molecular rotations for the pairs of compounds (*A*) represent therotational contribution of all asymmetric centres except $C_{(10)}$. In the pairs Nos. 1, 2, 3, and 7 the other asymmetric centres are at $C_{(13)}$, $C_{(14)}$, $C_{(17)}$, and in the side-chain, and at $C_{(3)}$ (in Nos. 2

and 7). The averages in these cases should be very close to the molecular rotation of the similar *neo*ergosterol derivative in which there is no angular methyl group at $C_{(10)}$ and ring B is aromatic. The last column in the Table records the difference between the average $[M]_D$

TABLE 1.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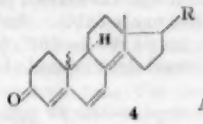
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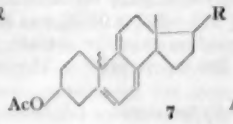
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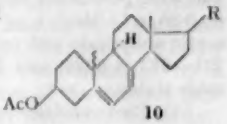
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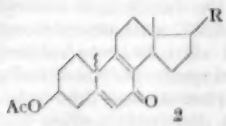
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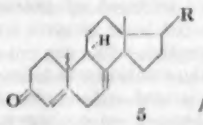
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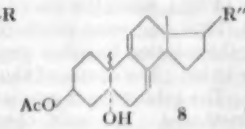
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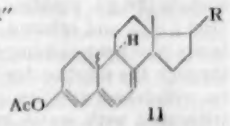
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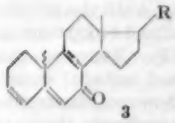
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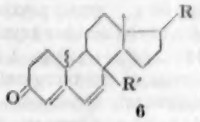
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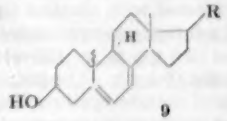

9

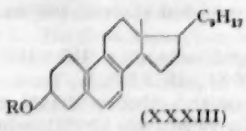
$R = C_9H_{17}$; $R'' = C_9H_{19}$.

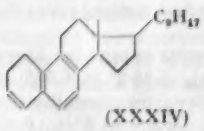
	Ketones						Other compounds				
	Lumisterol series	Ergosterol series	Diff.*	Aver.† (*A*)	*A* − $[M]_D^{neo}$		Lumisterol series	Ergosterol series	Diff.*	Aver.† (*A*)	*A* − $[M]_D^{neo}$
1	−3220° [1]	+2940° [2]	+6160°	−142°	−327°	7	+980° [1,8]	+890° [9]	−90°	+835°	+650°
2	−421 [1]	−136 [4]	+285	−279	−237	8	+329 [1]	+292 [10]	−37	+310	—
3	+321 [1]	−680 [4]	−1001	−180	−365	9	+758 [1]	−538 [11]	−1296	+110	—
4	−3000 [1]	+2300 [3,3]	+5300	−350	—	10	+571 [1]	−394 [12]	−965	+88	—
5	+150 [5]	−3 [6,7]	−153	+69	—	11	+1280 [1,8]	−625 [6]	−1905	+328	—
6	−1520 [1] (R′ = OH)	−94 [6] (R′ = H)	+1426	−807	—						

* Diff. = $[M]_D^{\beta} - [M]_D^{\alpha}$. † Aver. (*A*) = $([M]_D^{\alpha} + [M]_D^{\beta})/2$.

[1] Present work. [2] Elks, *J.*, 1954, 468. [3] Barton and Bruun, *J.*, 1951, 2728. [4] Elks, Evans, Long, and Thomas, *J.*, 1954, 451; Elks, Evans, Oughton, and Thomas, *J.*, 1954, 463. [5] Heilbron, Kennedy, Spring, and Swain (*J.*, 1938, 869) record $[\alpha]_D$ +48·7° for this compound. In our hands the compound prepared from lumisterol either with acetone and aluminium *tert.*-butoxide or *cyclo*hexanone and aluminium *iso*propoxide had a lower rotation {$[\alpha]_D$ +34·5° (*c*, 0·745) and $[\alpha]_D$ +32·3° (*c*, 0·595), respectively}. [6] Heilbron, Kennedy, Spring, and Swain, *loc. cit.* [7] Oppenauer, *Rec. Trav. chim.*, 1937, **56**, 137. [8] Heilbron, Spring, and Stewart, *J.*, 1935, 1221. [9] Honigmann, *Annalen*, 1934, **508**, 89. [10] *J.*, 1952, 4883. [11] Callow, *Biochem. J.*, 1931, **25**, 79. [12] Bills and Honeywell, *J. Biol. Chem.*, 1928, **80**, 15.

for the pair and that of either *neo*ergosterol (XXXIII; R = H) {($[M]_D$ −42° (Bonstedt, *Z. physiol. Chem.*, 1929, **185**, 165)} (pairs 2 and 7) or *neo*ergostapentaene (XXXIV) {($[M]_D$ +185° (EtOH) (Cook and Haslewood, *Chem. and Ind.*, 1934, **53**, 507)} (pairs 1 and 3). In making these calculations the acetylation increment for *neo*ergosterol is neglected; it is probably small [cf. the acetylation increment for *epi-neo*ergosterol $\Delta[M]_D$ −12° (Windaus and Deppe, *Ber.*, 1937, **70**, 76)].


(XXXIII)


(XXXIV)

EXPERIMENTAL

M. p.s were determined on a Kofler hot stage. Unless otherwise stated, rotations were determined on chloroform solutions at room temperature (18—25°) in a 1-dm. tube, ultraviolet spectra were determined on solutions in specially purified ethanol (Bladon, Henbest, and Wood,

J., 1952, 2737) by use of Unicam SP 500 spectrophotometers, and infrared spectra on Nujol mulls with a Perkin-Elmer model 21 double-beam instrument with sodium chloride optics.

Alumina (Spence Type "H" or Type "O") was deactivated by the method of Farrar, Hamlet, Henbest, and Jones (*J.*, 1952, 2657). Light petroleum had b. p. 60—80°.

The lumisteryl 3 : 5-dinitrobenzoate used had m. p. 139—142°; hydrolysis with aqueous ethanolic potassium hydroxide gave lumisterol, m. p. 116—118°, $[\alpha]_D$ +187° (*c*, 1·3), +187° (*c*, 0·85 in $COMe_2$), $\lambda_{max.}$ 272—273 (ε 9053) and 280 mμ (ε 8486). Acetylation of the sterol with acetic anhydride and pyridine gave the acetate, m. p. 100·5—102°, $[\alpha]_D$ +131° (*c*, 0·93); $\lambda_{max.}$ 271—273 (ε 8920) and 280 mμ (ε 8460). The sterol deteriorated slowly, but the acetate was more stable.

(*A*) *Photo-oxidation Experiments.*—(a) *Lumisteryl acetate in refluxing ethanol.* Lumisteryl acetate (20 g.), pyridine (4 c.c.), eosin [50 c.c. of a filtered solution of the dye (1 g.) in ethanol (100 c.c.)], and ethanol (1250 c.c.) were irradiated from beneath by a 300-watt incandescent lamp (the heat causing the solution to reflux gently), while oxygen (8—11 l./hr.) was bubbled through the solution for 16 hr. The course of the reaction was followed spectrophotometrically on withdrawn samples. The solution was evaporated under reduced pressure and the residue triturated with warm methanol. The solid obtained on cooling was dissolved in ether and methylene chloride and treated with alumina (*ca.* 50 g.; small portions) until the solution was colourless. The filtered solution was evaporated and the residue crystallised twice from acetone yielding feathery needles (3·5 g.), m. p. 155—157°, $[\alpha]_D$ +42° (*c*, 1·215). Evaporation of the mother liquors gave a solid (5·1 g.). The properties of the recrystallised material agreed with those of the pure lumisteryl acetate epidioxide ultimately obtained. However, discrepancies in the constants for different preparations suggested that it was impure. Accordingly, the crystalline material (material I) in light petroleum and benzene mixture (1 : 1; 200 c.c.), and the residue from the mother liquors (material II) in light petroleum (200 c.c.) were separately chromatographed on alumina (700 g. and 200 g., respectively). The chromatograms were eluted with light petroleum, benzene, ether, and methanol, and mixtures of these solvents, to give the following fractions (rotations measured in methylene chloride).

Material I: I*a*, $[\alpha]_D$ +252°; I*b*, $[\alpha]_D$ −9°; I*c*, $[\alpha]_D$ +30°; I*d*, $[\alpha]_D$ +41° to +56°; I*e*, $[\alpha]_D$ +61° to +72°; I*f*, $[\alpha]_D$ +26°.

Material II: II*a*, $[\alpha]_D$ +143° to +217°; II*d*, $[\alpha]_D$ +84° to +46°; II*e*, $[\alpha]_D$ +74·5° to +83·5°; II*g*, −31·3° to −47·5°; II*h*, $[\alpha]_D$ +40° to +44°; II*j*, $[\alpha]_D$ −7·4°.

Treatment of Bulked Fractions from the Chromatograms.—Fractions I*a* and II*a* after several crystallisations from ethyl acetate yielded needles of dehydrolumisteryl acetate (II), m. p. and mixed m. p. 141—144°, $[\alpha]_D$ +229° (*c*, 0·72). An authentic specimen prepared by Heilbron, Spring, and Stewart's method (*J.*, 1935, 1221), had m. p. 143—146°, $[\alpha]_D$ +236° (*c*, 1·55), $\lambda_{max.}$ 309—312 (ε 10,100) and 319—320 mμ (ε 10,800), and had an identical infrared spectrum (Found: C, 82·55; H, 9·95. Calc. for $C_{30}H_{44}O_2$: C, 82·5; H, 10·15%).

Fraction I*b* yielded needles (108 mg.; from acetone) of 3β-*acetoxy*-5β : 8β-*epidioxylumista*-6 : 9(11) : 22-*triene* (*dehydrolumisteryl acetate* β-*epidioxide*) (III; R = Ac), m. p. 178—180°, $[\alpha]_D$ −10·4° (*c*, 0·49) (Found: C, 76·85; H, 9·5. $C_{30}H_{44}O_4$ requires C, 76·9; H, 9·5%).

Fraction I*c* gave needles (270 mg.; from acetone), m. p. 165—167°, $[\alpha]_D$ +33·4° (*c*, 0·77), identified by alkali treatment (see below) as a mixture of the β-epidioxides of dehydrolumisteryl acetate (III; R = Ac) and lumisteryl acetate (IV; R = Ac) (Found: C, 76·2; H, 9·8%).

Fractions I*d* (4 subfractions) gave 3β-*acetoxy*-5β : 8β-*epidioxylumista*-6 : 22-*diene* (*lumisteryl acetate* β-*epidioxide*) (IV; R = Ac) (total yield, 1·948 g.; from acetone), m. p. 156—159°, 157—158°, 154—156°, 157—158°, $[\alpha]_D$ +46·3° (*c*, 0·62), +45·5° (*c*, 0·99), +45·8° (*c*, 0·88), +49·1° (*c*, 0·735) (Found: C, 76·7; 76·65; 76·75; 76·95; H, 9·65, 10·0, 9·95, 9·9. $C_{30}H_{46}O_4$ requires C, 76·55; H, 9·85%). All samples showed identical infrared spectra. On prolonged heating above its first melting point this compound solidified at about 160° to rosettes remelting at 169—172°.

Fraction II*d* gave impure lumisteryl acetate β-epidioxide, m. p. 157—159° (475 mg.; thrice from acetone), $[\alpha]_D$ +35·2° (*c*, 1·665) (Found: C, 76·85; H, 9·85%).

Fraction I*e* gave, on crystallisation from acetone and ether–methanol, needles (103 mg.), m. p. 152—155°, $[\alpha]_D$ +54·6° (*c*, 0·52) (Found: C, 79·95; H, 10·0%), which were probably impure lumisteryl acetate β-epidioxide.

Fraction II*e* had m. p. 145—170° even after four recrystallisations from acetone; it was probably a mixture of lumisteryl acetate β-epidioxide and dehydrolumisteryl acetate α-epidioxide.

Fraction II*g* gave 3β-*acetoxylumista*-5 : 8(9) : 22-*trien*-7-*one* (VI; R = Ac), needles (77 mg.;

second crop, 120 mg.) (from *iso*propyl ether), m. p. 179—182°, $[\alpha]_D$ −93·8° (*c*, 0·82) (Found: C, 79·7; H, 9·8. $C_{30}H_{44}O_3$ requires C, 79·6; H, 9·8%). Light absorption: $\lambda_{max.}$ 246 mμ, ε 11,800. Infrared spectrum (in Nujol): $\nu_{max.}$ 1725 s (OAc); 1663 s, 1631 s, 1597 m, (C:C·CO·C:C); 1250 s (OAc), 987 m (−C:C:CO·C:C) (see also Table 2).

Fractions I*f*, II*h*, and II*j* were not examined.

(b) *Lumisteryl acetate in ethanol at room temperature.* Lumisteryl acetate (5 g.) in ethanol (400 c.c.), ethanolic eosin [100 c.c.; as described in (a)], and pyridine (2·5 c.c.) were contained in a vertical Pyrex glass tube (70 cm. × 3·8 cm.) sealed at the lower end. Oxygen (4—6 l./hr.) was passed through the solution from the bottom, and the tube was irradiated by a 40 w "natural" type fluorescent tube, the distance between the centres of the reaction tube and the fluorescent tube being 7 cm. Oxygen flow and irradiation were continued for 24 hr.; by then the lumisteryl acetate concentration had been reduced by *ca.* 90%, as measured spectrographically. Solid separated from the mixture towards the end. The mixture was evaporated to dryness under reduced pressure, benzene being added towards the end. A solution of the residue in benzene (200 c.c.) was filtered on to alumina (500 g.), and the column eluted with benzene and ultimately with ether to give the following fractions (in order of elution).

Fraction III*a* ($[\alpha]_D$ +222°), giving needles of dehydrolumisteryl acetate (II) (420 mg.) (from ethyl acetate), m. p. 140—142°.

Fraction III*d* ($[\alpha]_D$ +52·5° to +43·5°), lumisteryl acetate β-epidioxide (IV; R = Ac) (1835 mg.; needles from acetone), m. p. 155—159°, $[\alpha]_D$ +48·5°.

Fraction III*g* ($[\alpha]_D$ −15° to −50°), 3β-acetoxylumista-5 : 8 : 22-trien-7-one (VI; R = Ac) (377 mg.; from *iso*propyl ether), m. p. 175—181°.

The above chromatogram is typical of many that were run. Increase in the quantity of alumina (to 1500 g.) allowed a sharper separation of the various fractions, but did not increase the final yields. Use of alumina which had not been deactivated caused extensive deacetylation and rearrangement of the peroxide. The dehydrolumisteryl acetate was eluted with benzene, but further elution with benzene did not give more material. Benzene–ether mixtures eluted materials having high rotations ($[\alpha]_D$ +60° to +100°). Finally, elution with 9 : 1 ether–methanol gave 5β : 8β-*epidioxy*-3β-*hydroxylumista*-6 : 22-*diene* (IV; R = H), leaflets (from methanol), m. p. 142—144°, $[\alpha]_D$ +72·7° (*c*, 0·73) (Found: C, 78·55; H, 10·4. $C_{28}H_{44}O_3$ requires C, 78·45; H, 10·35%). $\nu_{max.}$ (in Nujol) 3520 m (OH), 1635 w (Δ^6), and 983 m cm.$^{-1}$ (Δ^{22}). Acetylation gave the 3β-acetate as needles (from acetone), m. p. 150—153°, $[\alpha]_D$ +47·5° (*c*, 0·65) (Found: C, 76·8; H, 10·0. Calc. for $C_{30}H_{44}O_4$: C, 76·55; H, 9·85%). The infrared spectrum was identical with that of material from fraction I*d*.

(c) *Dehydrolumisteryl acetate in refluxing ethanol.* Dehydrolumisteryl acetate (500 mg.), ethanol (37·5 c.c.), pyridine (0·25 c.c.), and ethanolic eosin [12·5 c.c.; prepared as described in (a)] were irradiated in oxygen as in (a) (flow rate, 5 l./hr.; 300-watt incandescent lamp) for 9·5 hr. Spectrographic examination showed that the reaction was nearly complete after 3·5 hr. The mixture was evaporated to dryness under reduced pressure, and the residue was chromatographed in light petroleum–benzene (3 : 2; 200 c.c.) on alumina (100 g.), giving: (i) Dehydrolumisteryl acetate β-epidioxide (III; R = Ac) (from acetone–methanol), m. p. 178—179°, $[\alpha]_D$ −7·6° (Found: C, 77·0; H, 9·8. Calc. for $C_{30}H_{44}O_4$: C, 76·9; H, 9·5%); this material had an infrared spectrum identical with the material from fraction I*b*. (ii) 3β-*Acetoxy*-5α : 8α-*epidioxylumista*-6 : 9(11) : 22-*triene* (*dehydrolumisteryl acetate α-epidioxide*) (V; R = Ac), plates (from acetone–methanol), m. p. 164—166°, $[\alpha]_D$ +76·7° (*c*, 0·43) (Found: C, 76·8; H, 9·9. $C_{30}H_{44}O_4$ requires C, 76·9; H, 9·5%).

(d) *Dehydrolumisteryl acetate at room temperature.* Dehydrolumisteryl acetate (1·5 g.) in ethanol (400 c.c.), pyridine (2·5 c.c.), and eosin (100 c.c. of nominal 1% solution) was irradiated and oxygenated in the apparatus described in (b) for 21 hr. (oxygen rate, 4—5 l./hr.). The solution was evaporated to dryness under reduced pressure and the residue was chromatographed on alumina (200 g.). No clean separation of the two epidioxides was observed even when the epidioxide fractions (all solid; eluted with benzene; 1·34 g., $[\alpha]_D$ +54° to +70°) were rechromatographed. Fractional crystallisation of the mixture from ethanol gave dehydrolumisteryl acetate α-epidioxide (V; R = Ac) as needles (427 mg.), m. p. 166—169°, $[\alpha]_D$ +76·2° (*c*, 1·11), +79·5° (*c*, 0·83) (Found: C, 76·7; H, 9·25. Calc. for $C_{30}H_{44}O_4$: C, 76·9; H, 9·5%). This sample had higher m. p. and different crystal form from that described in (c) (ii) above; however, the m. p.s were not depressed when the samples were mixed, and the infrared spectra (Nujol mulls) were identical.

Material (920 mg.) from the mother liquors was refluxed in ethanol (20 c.c.) with potassium hydroxide (1 g.) in water (5 c.c.) for 1 hr. Acidification with concentrated hydrochloric acid and

extraction with ether gave a brownish product which was chromatographed in benzene on alumina (100 g.). Benzene eluted traces of oil; benzene–ether (9 : 1) gave a fraction (IV*a*; 113 mg.; for the examination of this material see section *D*). Benzene–ether (4 : 1 and 1 : 1) eluted material (IV*b*; 405 mg.) which after three recrystallisations from acetone–methanol gave 5α : 8α-*epidioxy*-3β-*hydroxylumista*-6 : 9(11) : 22-*triene* (V; R = H) (28 mg.), m. p. 155—157°, $[\alpha]_D$ +70·1° (*c*, 0·525) (Found: C, 78·4; H, 9·7. $C_{28}H_{42}O_3$ requires C, 78·8; H, 9·9%). The poor yield is due to the instability of the compound in methanolic solution.

Hydrolysis of the acetate α-epidioxide (20 mg.) gave a poor yield of the 3-hydroxy-compound, m. p. and mixed m. p. 148—153° $[\alpha]_D$ +70° (*c*, 0·1), having an infrared spectrum identical with the sample described above.

(*B*) *Lumisteryl Acetate* β-*Epidioxide.*—8β-*Hydroxylumista*-4 : 6 : 22-*trien*-3-*one* (XX). Lumisteryl acetate β-epidioxide (500 mg.) in ethanol (20 c.c.) and potassium hydroxide (1 g.) in water (5 c.c.) were heated under reflux for 2·5 hr. After cooling, the product was extracted with ether; concentration of the extract and treatment of the residue with methanol gave a solid (451 mg.), which (520 mg.) was chromatographed in benzene on alumina (50 g.). Benzene eluted traces of oil; benzene–ether (9 : 1 to 1 : 1) eluted material (460 mg.) from which was obtained 8β-*hydroxylumista*-4 : 6 : 22-*trien*-3-*one*, pale cream needles, m. p. 137—140°, $[\alpha]_D$ −377° (*c*, 0·45), −354° (*c*, 0·38 in MeOH) (Found: C, 80·6; H, 10·4. $C_{28}H_{42}O_2$,0·5MeOH requires C, 80·3; H, 10·4%), $\lambda_{max.}$ 283—285 mμ (ε 26,600). A satisfactory analysis for the unsolvated material was obtained only after sublimation at 170—190°/10^{-4} mm., which process did not remove the hydroxyl group. The sublimed material had m. p. 125—130°, resolidifying to hair-like needles, m. p. 142—145° (Found: C, 82·1; H, 10·35. $C_{28}H_{42}O_2$ requires C, 81·9; H, 10·3%), $\lambda_{max.}$ 282—283 mμ (ε 25,600). The compound was unchanged when left overnight with acetic anhydride and pyridine.

Lumista-4 : 6 : 8(14) : 22-*tetraen*-3-*one* (XXI). (*a*) Lumisterol (5 g.), benzoquinone (10 g.; recrystallised from light petroleum), and dry toluene (60 c.c.) were distilled until water had been eliminated by entrainment, a solution of aluminium *tert.*-butoxide (10 g.) in toluene (50 c.c.) was added, and the mixture was refluxed for 50 min. The black solid was filtered off and washed with hot benzene. The filtrates were washed with dilute sulphuric acid, and aqueous potassium hydroxide, and aqueous ammonium sulphate, dried (Na_2SO_4), and concentrated to a dark red gum (2·5 g.). This was chromatographed in benzene (100 c.c.) on alumina (100 g.), benzene being used as eluant. The first 300 c.c. eluted only red oil. The next 350 c.c. eluted material which was rechromatographed on alumina in light petroleum. Elution of this chromatogram with light petroleum (460 c.c.) gave needles, m. p. 80—86° (252 mg., 5%; from methanol). Further recrystallisation gave *lumista*-4 : 6 : 8(14) : 22-*tetraen*-3-*one*, (XXI) as pale yellow needles, m. p. 86—88°, $[\alpha]_D$ −767° (*c*, 0·505), −740° (*c*, 0·53 in MeOH) (Found: C, 85·7; H, 10·2. $C_{28}H_{40}O$ requires C, 85·65; H, 10·3%); $\lambda_{max.}$ 285 (ε 8170), 350—358 mμ (ε 25,500). This compound gave a yellow solution with a green fluorescence when treated with perchloric acid in methanol.

(*b*) 8β-Hydroxylumista-4 : 6 : 22-trien-3-one (37 mg.) in methanol (3 c.c.) was treated with perchloric acid (60% aqueous solution; 2 drops). The solution became yellow with a green fluorescence, $[\alpha]_D$ changing from −354° to −715° during 50 min. It was set aside for 1 hr. and then diluted with water, and the product (36 mg.) isolated by ether extraction. The pale yellow needles (from methanol) of the tetraenone had m. p. 86—89°, undepressed with material prepared as in (*a*), $[\alpha]_D$ −781° (*c*, 0·64), $\lambda_{max.}$ 284—286 (ε 7950), 354—358 mμ (ε 24,300). The infrared spectra (in Nujol) of the two samples were identical.

Lumista-4 : 6 : 8(14) : 22-*tetraen*-3-*one* 2 : 4-*dinitrophenylhydrazone*, prepared from the parent ketone or from 8β-hydroxylumista-4 : 6 : 22-trien-3-one, formed deep red plates, m. p. 264—265° (sintering 200°) (Found: C, 71·15; H, 7·9; N, 9·75. $C_{34}H_{44}O_4N_4$ requires C, 71·3; H, 7·7; N, 9·8%), $\lambda_{max.}$ 267·5 (ε 15,200), 335 (ε 16,400), 350 (ε 16,000), and 427·5 mμ (ε 42,450) in chloroform.

Lumista-4 : 6 : 8(9) : 22-*tetraen*-3-*one* (XXII). 8β-Hydroxylumista-4 : 6 : 22-trien-3-one (110 mg.) was refluxed with pyridine (4 c.c.) and acetic anhydride (4 c.c.) for 2 hr. in an atmosphere of carbon dioxide. The excess of reagents was removed *in vacuo* and the residue chromatographed in light petroleum on alumina. The material (90 mg.) eluted with petroleum–benzene gave greenish-yellow plates (from acetone) of *lumista*-4 : 6 : 8(9) : 22-*tetraen*-3-*one*, m. p. 134—137° (depressed to 100—110° on admixture with starting material), $[\alpha]_D$ −822° (*c*, 0·415) (Found: C, 85·75; H, 10·2. $C_{28}H_{40}O$ requires C, 85·65; H, 10·3%), $\lambda_{max.}$ 244 (ε 17,900) and 393 mμ (ε 11,000).

3β-*Acetoxylumistane*-5β : 8β-*diol* (XXVII; R = Ac). Lumisteryl acetate β-epidioxide

(600 mg.) in ethyl acetate (50 c.c.) was shaken with pre-reduced platinum oxide catalyst (Adams's; 100 mg.) and hydrogen until absorption ceased (uptake, 103 c.c. at 772 mm. and 23·5°; calc. for 3 moles, 102 c.c.). The residue obtained on removal of the solvent was absorbed from light petroleum (80 c.c.) on alumina (60 g.). Elution with light petroleum, light petroleum–benzene (1 : 1) (600 c.c.), and benzene (400 c.c.) and crystallisation (twice) from acetone yielded 3β-*acetoxylumistane*-5β : 8β-*diol* (468 mg.) as plates, m. p. 173—175°, $[\alpha]_D$ +89·5° (*c*, 0·415) (Found: C, 75·6; H, 10·9. $C_{30}H_{52}O_4$ requires C, 75·6; H, 11·0%); $\nu_{max.}$ 3545 m and 3320 ms (both sharp peaks; OH groups), 1720 s (OAc), 1297 s, 1270 s, 1251 s, 1220 s (axial OAc), 1075 m 1055 w, 1039 m, 1020 m, and 1000 m (OH groups) cm.$^{-1}$ in Nujol. In subsequent preparations chromatography was dispensed with; crystallisation of the product (from 700 mg. of epidioxide) gave the diol, m. p. 170—175°, $[\alpha]_D$ +91° (*c*, 0·91) (534 mg.; 73·5%). Crystallisation of the diol from methanol gave needles, m. p. 150—173° with accompanying change of crystal form to plates. No chemical change had taken place for subsequent crystallisation from acetone gave plates, m. p. 170—175°. This property is attributed to the formation of a low-melting needle form which only slowly changes into the plate form on heating.

In an earlier experiment, epidioxide (300 mg.) yielded on chromatography a preliminary fraction (96 mg.) easily eluted with benzene. This was slightly impure 3β-acetoxylumist-7-en-5β-ol (XXVIII) (see below) forming needles (from methanol), m. p. 136—139°, $[\alpha]_D$ +43·5°. (Infrared spectrum was similar to that of the pure material.) Further elution gave the 3β-acetoxy-diol. This result is difficult to explain in view of the stability of the diol.

Lumistane-3β : 5β : 8β-*triol* (XXVII; R = H). The above diol monoacetate (100 mg.) was refluxed with potassium hydroxide (500 mg.) in ethanol (20 c.c.) and water (5 c.c.) for 2·5 hr. After adding water and cooling, the solid was filtered off (85 mg.), m. p. 213—220°. *Lumistan*-3β : 5β : 8β-*triol* formed needles (from methanol), m. p. 215—221° with sublimation at 210°, $[\alpha]_D$ +97° (*c*, 0·65) (Found: C, 77·7; H, 11·65. $C_{23}H_{50}O_3$ requires C, 77·35; H, 11·6%); $\nu_{max.}$ 3325 and 3340 cm.$^{-1}$ (hydroxy bands) in Nujol. The triol was reacetylated to the diol monoacetate, m. p. and mixed m. p. 170—175°, $[\alpha]_D$ +92·6° (*c*, 0·75), possessing an infrared spectrum identical with that of an authentic specimen.

3β-*Acetoxylumist*-7-*en*-5β-*ol* (XXVIII). Refluxing of 3β-acetoxylumistane-5β : 8β-diol with acetone–acetic acid (19 : 1) for 3 hr. led to quantitative recovery of material; more acidic conditions and higher temperature led to dehydration. The diol monoacetate (300 mg.) was heated with glacial acetic acid on the steam-bath for 2 hr. Evaporation under reduced pressure gave an oil which was chromatographed in light petroleum on alumina (25 g.). Elution with light petroleum–benzene (500 c.c.) yielded oily material (105 mg.). Elution with benzene (300 c.c.) and crystallisation from methanol gave needles (36 mg.) of 3β-*acetoxylumist*-7-*en*-5β-*ol*, m. p. 138—141°, $[\alpha]_D$ +30·4 (*c*, 0·74) (Found: C, 78·8; H, 10·95. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%); $\nu_{max.}$ 3550 (OH), 1730 s (OAc), 1297 w, 1259, 1235 s, and 1210 m cm.$^{-1}$ (all axial OAc) in Nujol.

(*C*) *Dehydrolumisteryl Acetate α-Epidioxide.—Hydrogenation of dehydrolumisteryl 5α : 8α-epidioxide acetate.* (*a*) The epidioxide (70 mg.) in ethyl acetate (12·5 c.c.) was hydrogenated in the presence of pre-reduced platinum oxide (Adams's; 50 mg.) until absorption became slow (15 min.; 8·2 c.c. at 763 mm. and 23°. Calc. for 3 moles; 10·7 c.c.). The syrupy residue was dissolved in methanol (1 c.c.) at 60° and treated with concentrated hydrochloric acid (2 drops) for 2 min. Cooling, addition of water, ether extraction of the precipitate, and crystallisation from aqueous methanol gave 3β-*acetoxylumista*-7 : 9(11)-*dien*-5α-*ol* (XXX; R = Ac), hard granules, apparently isotropic, m. p. 155—158°, $[\alpha]_D$ +71·7° (*c*, 0·58) (Found: C, 79·0; H, 10·7. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%); $\lambda_{max.}$ 241 mμ (ε 17,300), $\lambda_{infl.}$ 235—236 mμ (ε 15,870). Hydrolysis of the material in the mother-liquors gave *lumista*-7 : 9(11)-*diene*-3β : 5α-*diol* (XXX; R = H) as plates (from methylene chloride–methanol), m. p. 255—263° (decomp.; change of form to needles at 220—230°), $[\alpha]_D$ +101° (*c*, 0·3 in C_5H_5N) (Found: C, 81·65; H, 11·3. $C_{28}H_{46}O_2$ requires C, 81·1; H, 11·2%); $\lambda_{max.}$ 240 mμ (ε 13,350), $\lambda_{infl.}$ 234·5 mμ (ε 12,400). This compound was sparingly soluble in most solvents and separated as a gel unless methanol was present.

(*b*) The epidioxide (300 mg.) in ethyl acetate (25 c.c.) was hydrogenated in the presence of pre-reduced platinum oxide (Adams's; 100 mg.) until absorption ceased (1·5 hr.; 57 c.c. absorbed at 742 mm. and 22°. Calc. for 4 moles, 62 c.c.). Several recrystallisations of the residue from methanol gave 3β-*acetoxy*-9β-*lumist*-7-*en*-5α-*ol* (XXXI; R = Ac) as needles (37 mg.), m. p. 147—148·5°, $[\alpha]_D$ −40·3° (*c*, 0·72) (Found: C, 78·8; H, 10·7. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%); $\nu_{max.}$ 3500 m (OH), 1716 s (OAc), and 1283 s cm.$^{-1}$ (equatorial OAc) in Nujol.

9β-*Lumist-7-ene*-3β : 5α-*diol* (XXXI; R = H). The above acetate (65 mg.) was refluxed with potassium hydroxide (200 mg.) in water (0·25 c.c.), methanol (3 c.c.), and dioxan (3 c.c.) for 45 min., and the mixture then cooled, diluted, and extracted with methylene chloride. Crystallisation from methanol and then from tetrahydrofuran–methanol afforded 9β-*lumist-7-ene*-3β : 5α-*diol* as plates changing to needles at *ca.* 200°, m. p. 231—237°, $[\alpha]_D$ +33·6° (*c*, 0·53 in C_5H_5N) (Found, on material sublimed at 200°/10^{-6} mm.: C, 80·35; H, 11·2. $C_{28}H_{46}O_2$ requires C, 80·7; H, 11·6%). This material is characterised by relative insolubility in organic solvents; it tended to separate from hot solvent as a gel, unless methanol was present.

(*D*) *Dehydrolumisteryl Acetate* β-*Epidioxide.—Action of alkali on dehydrolumisteryl acetate* β-*epidioxide* (III; R = Ac). The epidioxide (93 mg.) in ethanol (10 c.c.) and potassium hydroxide (0·5 g.) in water (2·5 c.c.) were refluxed for 2 hr., then cooled, diluted with water, and extracted with ether. The ethereal extract was washed with water and aqueous potassium hydrogen carbonate, dried, and evaporated. The residual red oil (88 mg.) was chromatographed in light petroleum on alumina (10 g.); elution with light petroleum–benzene mixture and with benzene gave oily material (21 mg.), benzene–ether (9 : 1) eluted a syrupy material (48 mg.) which would not crystallise, and further elution gave only traces of non-crystalline material. The material eluted by benzene–ether was probably impure 8β-hydroxylumista-4 : 6 : 9(11) : 22-tetraen-3-one (XXV). It had $[\alpha]_D$ −344° (initial) ⟶ −209° (1 hr.) (*c*, 0·48 in CH_2Cl_2); $\lambda_{max.}$ 285—286 mμ (ε 14,300). When perchloric acid (1 drop) was added to the spectrographic solution the spectrum changed (24 hr.) to $\lambda_{max.}$ 296 (ε 13,450) and 385 mμ (ε 10,500). On the basis of these values and those of the pure pentaenone (see below) the 8β-hydroxy-ketone was 81·5% pure. The calculated value of the maximal extinction coefficient of the pure 8β-hydroxy-ketone is then 17,600.

Evaporation of the methylene chloride solution used in the determination of the rotation gave a yellow oil which rapidly solidified. To ensure complete dehydration it was dissolved in methanol (2 c.c.), and aqueous perchloric acid (60%; 2 drops) added. The red solution was then immediately worked up and gave *lumista*-4 : 6 : 8(14) : 9(11) : 22-*pentaen*-3-*one* (XXVI) (46 mg.) as bright yellow prisms (16 mg.), m. p. 142—145° (from methanol), $[\alpha]_D$ −285° (*c*, 0·56) (Found: C, 86·15; H, 9·7. $C_{28}H_{38}O$ requires C, 86·1; H, 9·8%); $\lambda_{max.}$ 300 (ε 16,300) and 385—386 mμ (ε 13,100).

Fraction IV*a* (see above) after three recrystallisations from methanol gave more lumista-4 : 6 : 8(14) : 9(11) : 22-pentaen-3-one (40 mg.), m. p. 142—145°, $[\alpha]_D$ −279° (*c*, 0·5).

(*E*) 3β-*Acetoxylumista*-5 : 8(9) : 22-*trien*-7-*one* (VI; R = Ac).—*Hydrolysis of* 3β-*acetoxylumista*-5 : 8(9) : 22-*trien*-7-*one*. The ketone (220 mg.) in ethanol (15 c.c.) was treated with potassium hydroxide (1 g.) in water (1 c.c.) and ethanol (5 c.c.), and set aside at room temperature overnight. Dilute hydrochloric acid was then added and the precipitate washed with water and dried (206 mg.). Crystallisation from acetone gave 3β-*hydroxylumista*-5 : 8(9) : 22-*trien*-7-*one*, as plates, m. p. 233—237° (decomp.; change of form below m. p.), $[\alpha]_D$ −93·0° (*c*, 0·71), −93·5° (*c*, 0·43) (Found: C, 81·85; H, 10·45. $C_{28}H_{42}O_2$ requires C, 81·9; H, 10·3%), $\lambda_{max.}$ 250 mμ (ε 12,800), $\nu_{max.}$ 3365 (OH), 1652 s, 1600 s, 1605 sh, and 875 m cm.$^{-1}$ (C:C–CO–C:C). Acetylation with acetic anhydride and pyridine at room temperature overnight gave the 3β-acetate, m. p. and mixed m. p. 180—183°, having infrared spectrum identical with that of authentic material. The residue obtained on evaporation of the mother liquor from the hydrolysis (132 mg.; $[\alpha]_D$ −20° in methylene chloride) was refluxed with potassium hydroxide (1 g.) in ethanol (5 c.c.) and water (1 c.c.) for 2·5 hr. Working up gave a dark red oil (101 mg.) which was dissolved in benzene (100 c.c.) and passed through alumina (10 g.). Evaporation of the eluates gave a solid (61 mg.) which yielded *lumista*-3 : 5 : 8(9) : 22-*tetraen*-7-*one* (VIII) as plates (acetone–methanol), m. p. 172—174° (change of form to needles below the m. p.), $[\alpha]_D$ +83·6° (*c*, 0·495) (Found: C, 85·6; H, 10·2. $C_{28}H_{40}O$ requires C, 85·65; H, 10·3%); $\lambda_{max.}$ 272—273 mμ (ε 13,800), $\lambda_{infl.}$ 302—305 mμ (ε 8100), $\nu_{max.}$ 1639 s, 1605 m, 1589 m, and 880 s cm.$^{-1}$ (–C:C–C:C–CO–C:C–) in Nujol (see below).

The same material was obtained from the hydrolysis of the mother liquors from the crystallisations of 3β-acetoxylumista-5 : 8(9) : 22-trien-7-one and of lumisteryl acetate β-epidioxide.

Treatment of 3β-*acetoxylumista*-5 : 8(9) : 22-*trien*-7-*one with zinc, acetic acid, and silver nitrate*. The ketone (100 mg.) was refluxed with zinc dust (1 g.) and silver nitrate (100 mg.) in acetic acid (5 c.c.) for 1 hr. The zinc was filtered off and washed with methylene chloride, and the filtrates extracted with ether. Evaporation of the extracts, dissolution of the residue (100 mg.) in 2 : 1 light petroleum–benzene (30 c.c.), chromatography on alumina (10 g.) and elution, first with light petroleum–benzene (oily material) and then with benzene, gave (?)-*acetoxyanthraergosta*-5 : 7 : 9 : 22-*tetraen*-7-*ol* (VII) as flakes (from acetone), m. p. 215—218° (with change to needles

below m. p.), $[\alpha]_D$ −38° (*c*, 0·39) (Found: C, 79·5; H, 9·75. $C_{30}H_{44}O_3$ requires C, 79·6; H, 9·8%); $\lambda_{max.}$ (at pH 7) 290 mμ (ε 2930), $\lambda_{max.}$ (at pH 9·5) 304—306 mμ (ε 3600); $\nu_{max.}$ 3445 s (OH), 1710 s (OAc), 1600 m and 1589 m (phenol), 1267 s (OAc), and 828 m cm.$^{-1}$ (Δ^{23}). This material was not soluble in aqueous potassium hydroxide and did not colour aqueous or ethanolic ferric chloride.

3β-*Acetoxyergosta*-5 : 8(9)-*dien*-7-*one* (X). 3β : 11α-Diacetoxyergosta-5 : 8(9)-dien-7-one (500 mg.) was heated with zinc dust (1 g.), glacial acetic acid (20 c.c.), and a few drops of aqueous silver nitrate for 1 hr. The zinc was filtered off and the product (500 mg. crude) crystallised from acetone–methanol, affording plates of 3β-*acetoxyergosta*-5 : 8(9)-*dien*-7-*one*, m. p. 185—186°, $[\alpha]_D$ −40·7° (*c*, 0·935), −39·7° (*c*, 0·59) (Found: C, 79·0; H, 10·2. $C_{30}H_{46}O_3$ requires C, 79·25; H, 10·2%); $\lambda_{max.}$ 244 mμ (ε 11,600); $\nu_{max.}$ 1728 s (OAc), 1664 s, 1630 ms, 1596 mw (all C=C–CO–C=C), and 1267 s cm.$^{-1}$ (OAc) in Nujol.

(?)-*Acetoxyanthraergosta*-5 : 7 : 9-*trien*-7-*ol* (XI). (*a*) 3β-Acetoxyergosta-5 : 8(9)-dien-7-one (200 mg.), zinc dust (1 g.), silver nitrate (230 mg.), and acetic acid (10 c.c.) were refluxed for 0·5 hr. More (1 g.) zinc was added and refluxing continued for a further 0·5 hr. The product was chromatographed on alumina (10 g.); benzene eluted (?)-*acetoxyanthraergosta*-5 : 7 : 9-*trien*-7-*ol* (32 mg.), which formed flakes, m. p. 210—215°, $[\alpha]_D$ −31·5° (*c*, 0·385) (Found: C, 79·45; H, 10·25. $C_{30}H_{46}O_3$ requires C, 79·25; H, 10·2%); $\lambda_{max.}$ (at pH 7) 288—289 mμ (ε 2785), $\lambda_{max.}$ (at pH 9·5) 304 mμ (ε 3260); $\nu_{max.}$ 3440 s (OH), 1714 s (OAc), 1602 m and 1592 m (phenol), and 1269 s cm.$^{-1}$ (OAc) in Nujol.

(*b*) (?)-Acetoxyanthraergosta-5 : 7 : 9 : 22-tetraen-7-ol (11 mg.) and Adams's platinum oxide catalyst (50 mg.), in ethyl acetate (10 c.c.), were shaken in hydrogen for 1 hr. Isolation of the product gave (?)-acetoxyanthraergosta-5 : 7 : 9-trien-7-ol as flakes, m. p. 210—213° undepressed on admixture with material prepared as in (*a*), $[\alpha]_D$ −26° (*c*, 0·43). The identity of the samples prepared in (*a*) and (*b*) was confirmed by their identical infrared spectra and the similar behaviour of their solidified melts under the polarising microscope (observation kindly made by Dr. J. D. Bu'Lock).

Infrared Spectra of Ketones.—The spectra of seven of the ketones described above were determined in carbon disulphide at a concentration of 14 mg./c.c. and path length 2 mm. in the regions 1800—1500 and 1300—660 cm.$^{-1}$. The results are recorded in Table 2. Carbon disulphide absorbs strongly in the regions 1650—1400 and 900—800 cm.$^{-1}$ obscuring important peaks; results in these regions are taken from the routine spectra obtained as Nujol mulls (figures for these regions are in parentheses). All the compounds show strong absorption at maxima associated with the stretching vibrations in the conjugated carbonyl group (1670—

TABLE 2. *Infrared spectra of ketones in the lumisterol series.*

Compound	Wave-numbers of principal peaks (cm.$^{-1}$)
1. Lumista-4 : 7 : 22-trien-3-one	**1674 s**, (1621 m), 1273 mw, 1230 mw, 1195 w, 1160 w, 1140 vw, 1125 vw, 1075 vw, 1030 vw, 975 m, 960 w, (857 s), 825 w, 805 w, 765 w.
2. 8β-Hydroxylumista-4 : 6 : 22-trien-3-one	**1667 s**, (1627 s), (1580 m), 1295 w, 1275 m, 1230 m, 1200 mw, 1165 w, 1145 w, 1123 w, 1095 w, 1070 w, 1040 w, 1015 w, 995 m, 975 m, 947 m, 937 mw, 910 w, (885 s), 791 w, 770 w, 750 w, 730 w, 710 w, 675 w.
3. Lumista-4 : 6 : 8(14) : 22-tetraen-3-one	**1663 s**, (1635 w), (1590 s), 1299 w, 1270 m, 1230 m, 1215 mw, 1197 m, 1182 w, 1170 w, 1105 vw, 1070 vw, 1025 mw, 1010 vw, 975 m, 965 vw, (880 s), 800 w, 760 w, 695 w.
4. Lumista-4 : 6 : 8(9) : 22-tetraen-3-one	1655 s, (1575 m), (1550 m), 1275 mw, 1247 m, 1235 mw, 1197 mw, 1182 w, 1167 w, 1075 w, 1025 mw, 1007 w, 985 w, 974 m, 960 w, 957 m, 928 w, (869 s), 793 w, 773 w, 757 mw, 707 w, 680 w.
5. Lumista-4 : 6 : 8(14) : 9(11) : 22-pentaen-3-one	**1660 s**, (1590 s), (1565 w), 1287 w, 1260 m, 1233 ms, 1193 w, 1176 w, 1146 w, 1025 vw, 1030 w, 994 m, 975 m, 965 vw, 945 m, 930 m, (869 s), 815 w, 785 vw, 770 mw, 760 vw, 725 vw.
6. Lumista-3 : 5 : 8(9) : 22-tetraen-7-one	**1643 s**, (1605 m), (1589 m), 1275 mw, 1260 w, 1240 w, 1210 w, 1190 m, 1129 w, 1100 w, 1078 w, 1025 w, 985 mw, 973 m, 935 mw, (880 s), 778 w, 723 w, 685 w.
7. 3β-Acetoxylumista-5 : 8(9) : 22-trien-7-one	**1736 s**, **1663 s**, (1631 s), (1597 m), 1275 sh, 1245 s, 1223 ms, 1207 ms, 1182 mw, 1151 mw, 1079 w, 1023 ms, 1003 w, 987 mw, 973 mw, 955 w, 930 w, 915 w, (890 w), (876 w), (847 mw), (835 mw), 756 w, 720 w, 685 w.

Abbreviations, which also apply to the text: s, strong; ms, medium strong; m, medium; mw, medium weak; w, weak; vw, very weak; sh, shoulder.

1580 cm.$^{-1}$) and all except No. 7 show a strong peak at about 880 cm.$^{-1}$ which is characteristic of αβ-unsaturated ketones (cf. Elks, *J.*, 1954, 468). The absence of such a strong peak in the cross-conjugated ketone (No. 7) is probably due to the symmetrical disposition of the double bonds about the ketone group. All the compounds have a maximum (975 cm.$^{-1}$) corresponding to the olefinic out-of-plane bending vibration of the side-chain double bond. Compound No. 7 shows maxima associated with the acetate group (1736, and groups in the regions 1275—1225 and 1020 cm.$^{-1}$). The other peaks cannot be identified with any certainty (but see the recent paper of R. N. Jones and Herling, *J. Org. Chem.*, 1954, **19**, 1252).

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Studies of Organic Fluorine Compounds. Part IV. Synthesis of Esters of Fluoro-oxaloacetic and of Fluoropyruvic Acid.*

By I. BLANK, J. MAGER, and ERNST D. BERGMANN.

[Reprint Order No. 6012.]

Esters of fluoroacetic acid condense with alkyl oxalates in presence of alkali alkoxides to the alkali enolates of the esters of fluoro-oxaloacetic acid. These esters show a very low (8·9%) enol content. Hydrolysis of the esters to the free acid failed, the main reaction being fission to oxalic and fluoroacetic acid. Under suitable conditions, fluoropyruvic acid could be prepared in small yield by the fission. Both diethyl fluoro-oxaloacetate and fluoropyruvic acid are very much less toxic than the fluoroacetate.

The infrared spectra of the new compounds have been determined.

MUCH research has recently been devoted to the biological effects of fluoroacetate and related compounds (Martius, *Annalen*, 1949, **561**, 237; Peters, *Proc. Roy. Soc.*, 1952, **139**, *B*, 143; *Brit. Med. J.*, 1952, 1165). It has been shown that fluoroacetic acid is metabolised in the organism to fluorocitric acid, which eventually blocks the tricarboxylic acid cycle. It seemed, therefore, of interest to prepare the monofluoro-derivatives of the members of the citric acid cycle, to study their biological behaviour, and, in particular, to prepare diethyl fluoro-oxaloacetate as a prospective starting material for fluoropyruvic acid and a number of other substances. We have published short communications on the synthesis and biological properties of diethyl fluoro-oxaloacetate and fluoropyruvic acid (*Bull. Res. Council Israel*, 1953, **3**, 101; see also Mager and Blank, *Nature*, 1954, **173**, 126; Blank and Mager, *Experientia*, 1954, **10**, 77), and a synthesis of diethyl fluoro-oxaloacetate by essentially the same method has been described by Rivett (*J.*, 1953, 3710).

Wislicenus (*Ber.*, 1910, **43**, 3552) showed that diethyl oxalate condenses with ethyl chloroacetate, but not with ethyl bromoacetate, without loss of the halogen atom. Since the C–F bond is known to be the most stable of the halogen–carbon bonds (Swarts, *Bull. Soc. chim. France*, 1896, **15**, 1134; Glockler, in "Fluorine Chemistry," Academic Press Inc., New York, 1950, Vol. I, p. 314), it was expected, and has now been confirmed, that ethyl fluoroacetate would lend itself easily to Claisen condensation. Condensing ethyl fluoroacetate with diethyl oxalate in the presence of alcohol-free sodium ethoxide gave yields of about 80% of pure diethyl sodiofluoro-oxaloacetate, from which the free ester was easily

* Part I, *J.*, 1953, 3786; Parts II and III, *Proc. k. ned. Akad. Wetenschap.*, c, 1953, **56**, 423, 427. (The last two papers were erroneously numbered Parts I and II.)

prepared. Attempts, however, to prepare the free fluoro-oxaloacetic acid by hydrolysis with cold concentrated hydrochloric acid failed under conditions under which the fluorine-free parent compound yields oxaloacetic acid—albeit only in 5—8% yield—and pyruvic acid (as the main product) (cf. Wislicenus, *Annalen*, 1888, **246**, 327; see also "Biochemical Preparations," 1953, Vol. III, p. 59) ("ketonic fission" of oxaloacetic acid). From diethyl fluoro-oxaloacetate, only fluoropyruvic acid and large quantities of oxalic acid could be obtained. It seems that fluoro-oxaloacetic acid, being even less stable than oxaloacetic acid, decomposes immediately on formation. However, the main reaction is "acid fission," leading to oxalic and fluoroacetic acid: this reaction is brought about for the parent substance only by alkali (Wislicenus, *loc. cit.*).

In this respect, diethyl chloro-oxaloacetate occupies an intermediate position, since it yields much smaller amounts of oxalic acid on treatment with cold concentrated hydrochloric acid. (Dilute sulphuric acid gives oxalic and chloroacetic acid; Peratoner, *Gazzetta*, 1892, **22**, II, 38.) "Acid fission" of fluoro-oxaloacetic acid could not be appreciably prevented even under the very mild conditions adopted by Heidelberger and Hurlbert (*J. Amer. Chem. Soc.*, 1950, **72**, 4704) for the preparation of oxaloacetic acid, *viz.*, pyrolysis of its di-*tert.*-butyl ester. In this case, too, large amounts of oxalic acid, together with fluoropyruvic acid, were formed, and only minor quantities of the desired fluoro-oxaloacetic acid could be identified.

Di-*tert.*-butyl fluoro-oxaloacetate was prepared by the Claisen condensation of di-*tert.*-butyl oxalate with *tert.*-butyl fluoroacetate, dry potassium *tert.*-butoxide being the condensing agent. Both diethyl and di-*tert.*-butyl fluoro-oxaloacetate give a characteristic bluish-brown colour reaction with alcoholic ferric chloride solution, whereas the colour given by the non-fluorinated analogue is brown-red. This is in keeping with Henecka's findings (*Ber.*, 1948, **81**, 179) concerning the effect of halogen substitution on the colour of the ferric complex of β-diketones. The intensity of the colour is also much weaker than that obtained with equivalent amounts of the parent substance, owing to the low degree of enolisation characteristic of fluoro-oxaloacetates. The keto–enol equilibrium (enol %) was determined by Meyer's indirect method for the following diethyl esters in *n*-hexane: Oxaloacetate, 72—79; chloro-oxaloacetate, 24—27; fluoro-oxaloacetate, 8—9. According to Meyer (*Ber.*, 1912, **45**, 2860), dimethyl oxaloacetate occurs in the solid state and in light petroleum almost wholly as the enol.

Replacement of the hydrogen in the α-position of the oxaloacetate by a halogen atom decreases the enolisation, more so for fluorine than for chlorine. Similar results have been obtained in the acetoacetate series. Ethyl acetoacetate was found to contain 7·4% of enol in accordance with previous data (Meyer *et al.*, *Annalen*, 1911, **380**, 222; *Ber.*, 1911, **44**, 2720; 1914, **47**, 841), and the αγ-difluoro- and -dichloro-acetoacetate showed 5·2 and 5·4%, respectively. Although α-halogen atoms decrease the tendency to enolisation (ethyl α-bromoacetoacetate 4% enol; Meyer, *Annalen*, 1911, **380**, 241), halogen in the γ-position increases it; *e.g.*, Arndt, Loewe, and Capuano (*Rev. Fac. Sci. Istanbul*, 1943, **8**, *A*, 122) found for ethyl γ-chloro- and γγγ-trichloro-acetoacetate 10·9 and 40—50% enol, respectively. The pronounced ketonic character of diethyl fluoro-oxaloacetate makes it understandable that it undergoes the Reformatzky reaction with ethyl bromoacetate and zinc in the normal manner (Rivett, *loc. cit.*).

For the preparation of fluoropyruvic acid, we first attempted to hydrolyse fluoropyruvonitrile in a manner similar to that described by Tschelinzeff and Schmidt (*Ber.*, 1929, **62**, 2210), but always obtained complete decomposition. Fluoropyruvic acid was prepared, however, by treatment of diethyl fluoro-oxaloacetate with hot dilute hydrochloric acid, which led to concurrent hydrolysis and decarboxylation. Although the main reaction under these conditions is the "acid fission," giving a mixture of oxalic, fluoroacetic, and fluoropyruvic acid, the method described on p. 2193 gives pure fluoropyruvic acid as a colourless liquid crystallising at low temperature, but in only 9% yield; it is characterised by a well-crystallised semicarbazone. The methyl ester was prepared easily by means of diazomethane or of hydrogen chloride in anhydrous methanol at room temperature.

The toxicity of diethyl sodiofluoro-oxaloacetate and fluoropyruvic acid was tested on rats and mice. The former proved to be practically non-toxic (LD_{50} 750 mg./kg.); the

latter (as well as its methyl ester) was lethal at doses of about 80 mg./kg. The biological aspects of this study will be described elsewhere.

In the infrared, the carbonyl group of diethyl fluoro-oxaloacetate, fluoropyruvic acid, and methyl fluoropyruvate absorbs at 1738—1750 (broad band), 1723, and 1743 cm.$^{-1}$, respectively. The fluorine atom is responsible for peaks at 1094, 1035, and 1046 cm.$^{-1}$, respectively. These variations, and the observation that the C–F absorption in the semicarbazone of fluoropyruvic acid is shifted as far as 980 cm.$^{-1}$, will form the subject of a forthcoming publication. In fluoropyruvonitrile, the C≡N frequency was found at 2250 cm.$^{-1}$ and the carbonyl band at 1730 cm.$^{-1}$.

Experimental

Carbon and hydrogen determinations were carried out by Bodenheimer and Goldstein's method (*Bull. Res. Council Israel*, 1953, **3**, 53), and fluorine analyses by that of Eger and Yarden (*ibid.*, 1954, **4**, 305).

Diethyl Fluoro-oxaloacetate.—To a suspension of alcohol-free sodium ethoxide, prepared from metallic sodium (23 g.) in anhydrous ether (200 ml.), freshly distilled diethyl oxalate (146 g.) and after a few minutes ethyl fluoroacetate (106 g.) were added dropwise. The mixture was left overnight at room temperature, and the solid yellow enolate was filtered off, washed several times with ether until the filtrate was colourless, and dried (yield 180 g., 79%). The enolate is a cream-coloured, hygroscopic powder which becomes yellow on storage, is soluble in water and alcohol, insoluble in ether and hydrocarbons, and gives a bluish-brown colour reaction with alcoholic ferric chloride solution.

A solution of the enolate (100 g.) in cold water (50 ml.) was acidified with dilute sulphuric acid to a pH of 1—2 in the cold and extracted repeatedly with ether. The extract was dried (Na_2SO_4), and the solvent evaporated. The free diethyl fluoro-oxaloacetate (60 g., 67%) distilled at 120—122°/9 mm. as a colourless oil, soluble in alcohol and ether, insoluble in water and hydrocarbons. With alcoholic ferric chloride, it gives a deep bluish-brown colour; it has d_4^{20} 1·261, n_D^{20} 1·42, $[M]_R$ 41·44 (Calc.: 42·27) (Found: C, 46·7; H, 5·7. Calc. for $C_8H_{11}O_5F$: C, 46·6; H, 5·3%) (Rivett, *loc. cit.*, gives b. p. 99°/3 mm., n_D^{25} 1·4203). The 2 : 4-dinitrophenylhydrazone, recrystallised from alcohol, had m. p. 142° (Found: C, 44·0; H, 4·0; N, 13·9. Calc. for $C_{14}H_{15}O_8N_4F$: C, 43·5; H, 3·9; N, 14·5%) (Rivett, *loc. cit.*, gives m. p. 145°).

Acid Hydrolysis of Diethyl Fluoro-oxaloacetate and Chloro-oxaloacetate.—The fluoro-ester (50 g.) was shaken vigorously with concentrated hydrochloric acid (100 ml.) for 2 hr. and set aside at −15°. After 5 days, a white precipitate had been formed, and was filtered off and dried in a desiccator (yield *ca.* 4 g.). After recrystallisation from ethyl methyl ketone, it did not give a colour with ferric chloride or liberate carbon dioxide on treatment with aniline citrate in the Warburg apparatus. It gave a strong colour reaction for oxalic acid with diphenylamine (Feigl, "Qualitative Analysis by Spot Tests," Elsevier Publ. Co. Inc., New York, 1947), and was quantitatively precipitated from its aqueous solution by calcium acetate. Titration with potassium permanganate gave the value expected for anhydrous oxalic acid. In the mother-liquor left after the separation of this acid, the presence of fluoroacetic acid was indicated by the lanthanum nitrate reaction (Hutchens and Kass, *J. Biol. Chem.*, 1949, **177**, 571).

Oxalic acid was also detected in the hydrolysis products of diethyl chloro-oxaloacetate, but in much smaller quantity than from the equivalent amount of the fluoro-oxaloacetate.

tert.-*Butyl Fluoroacetate.*—This, prepared by a method similar to that of Westheimer and Shookhoff (*J. Amer. Chem. Soc.*, 1940, **62**, 269) for the chloroacetate, had b. p. 129·5—131°, d_4^{20} 0·9904, n_4^{20} 1·386, $[M]_R$ 32·04 (Calc.: 31·42) (Found: C, 54·2; H, 8·2. $C_6H_{11}O_2F$ requires C, 53·8; H, 8·2%).

Di-tert.-*butyl Fluoro-oxaloacetate.*—Dry potassium *tert.*-butoxide, from potassium (2·4 g.) and anhydrous *tert.*-butanol (75 ml.), was suspended in ether (50 ml.), and di-*tert.*-butyl oxalate (12·8 g.) (Backer and Homan, *Rec. Trav. chim.*, 1939, **58**, 1048) and *tert.*-butyl fluoroacetate (8 g.) were added successively, with shaking. After several minutes, a voluminous precipitate formed. After being kept overnight at room temperature, the di-*tert.*-butyl potassiofluoro-oxaloacetate was isolated as a white, very hygroscopic powder, soluble in water and alcohol, insoluble in hydrocarbons. The free ester, prepared from the enolate as for the diethyl compound (above), solidified at about 15°, and was soluble in benzene, chloroform, and ethyl acetate, insoluble in non-polar solvents. With alcoholic ferric chloride solution, it gives a very faint violet-red colour reaction. The 2 : 4-*dinitrophenylhydrazone*, recrystallised from alcohol,

formed needles, m. p. 137—138° (Found: C, 48·5; H, 5·4; N, 12·1. $C_{18}H_{23}O_8N_4F$ requires C, 48·9; H, 5·2; N, 12·7%).

*Hydrolysis of Di-*tert.*-butyl Fluoro-oxaloacetate.*—A solution of the ester (3 g.) in dry benzene (150 ml.) was subjected to azeotropic distillation until no more traces of water appeared in the distillate. Then a small quantity of toluene-*p*-sulphonic acid (0·2 g.) was added and the substance heated until gas evolution ceased (*ca.* 1·5 hr.). The solution was decanted from a small amount of amorphous yellowish deposit on the walls of the reaction vessel and cooled at 4° for 48 hr. The precipitate so obtained (300 mg.) was easily soluble in water and consisted mainly of oxalic acid. However, the aqueous solution of the crystals also gave a violet colour with ferric chloride and a precipitate with 2 : 4-dinitrophenylhydrazine. That these reactions are due to the presence, in the crystals, of some fluoro-oxaloacetic acid is demonstrated by the following observation: when the aqueous solution is heated on the water-bath for several minutes, the reaction with ferric chloride becomes negative, but the solution still gives a reaction with 2 : 4-dinitrophenylhydrazine, leading to the 2 : 4-dinitrophenylhydrazone of fluoropyruvic acid.

It was not possible to isolate pure fluoro-oxaloacetic acid from its mixture with an excess of oxalic acid.

Fluoropyruvonitrile.—Fluoroacetyl bromide. Phosphorus tribromide (95 g.) was added dropwise to fluoroacetic acid (70 g.) cooled in ice–water, and the mixture refluxed for 3 hr. and distilled. The fraction distilling at 85—95° was collected; on redistillation, it boiled at 87—88° (yield 60 g., 47%).

In a three-necked flask, cuprous cyanide (75 g.), dried at 110° for 3 hr., was added portionwise to fluoroacetyl bromide (90 g.), and the mixture heated in an oil-bath (120°) for 6 hr. Unchanged fluoroacetyl bromide was removed, and the residue distilled *in vacuo*; the product, b. p. 88—93°/20 mm. (yield 25%), did not give satisfactory analytical figures, but the infrared spectrum indicated that the desired nitrile had been formed.

Fluoropyruvic acid. A solution of diethyl sodiofluoro-oxaloacetate (200 g.) in a mixture of hydrochloric acid (*d* 1·12; 400 ml.) and water (600 ml.) was heated at 130°, with stirring, during 6 hr. The solution was concentrated *in vacuo* to 200 ml., cooled, and filtered, and the filtrate extracted with five 100-ml. portions of ether. The ether residue was fractionated; the acid distilled at 98°/5 mm. as a colourless liquid which solidified to a cream-white solid. It was freed from the last traces of oxalic acid by redissolving it in water, extracting the solution several times with ether, and renewed distillation, then having m. p. 50° (with slight previous sintering) (9·5 g., 9%) (Found: C, 34·0; H, 3·1%; equiv., 106. $C_3H_3O_3F$ requires C, 34·0; H, 2·8%; equiv., 106). *Fluoropyruvic acid* is very soluble in water, insoluble in hydrocarbons. It readily gives a *semicarbazone*, m. p. 205° (decomp.) (from *n*-butanol) (Found: C, 29·2; H, 3·8; N, 25·3. $C_4H_6O_3N_3F$ requires C, 29·4; H, 3·7; N, 25·7%). The purity of the acid was also assayed by Silverman and Werkman's manometric method (*J. Biol. Chem.*, 1941, **138**, 35): a solution of fluoropyruvic acid (1·36 mg., 12·8 μmole) was treated in a Warburg vessel with a saturated solution (0·5 ml.) of ceric sulphate in 2N-sulphuric acid at 37°. The amount of carbon dioxide evolved was 290 mm.³, exactly equivalent to 12·8 μmole.

Methyl fluoropyruvate. (*a*) To fluoropyruvic acid (8 g.) in dry ether (50 ml.), cooled in ice–salt, an excess of ethereal diazomethane was added. The ethereal solution was dried (Na_2SO_4) for 24 hr. and distilled (b. p. 85°/14 mm.; 5·5 g., 60%). (*b*) A current of dry hydrogen chloride was passed for 2 hr. through a solution of fluoropyruvic acid (18 g.) in anhydrous methanol (50 ml.). The excess of the methanol was distilled off, and the residue dissolved in ether (100 ml.). This solution was washed with water, sodium hydrogen carbonate solution, and again with water, and dried (Na_2SO_4). The fraction distilling at 85°/14 mm. was collected (yield 50%). *Methyl fluoropyruvate* is a colourless liquid, soluble in hydrocarbons, insoluble in water; n_D^{20} 1·423, d_{20}^{20} 1·510, $[M]_R$ 22·80 (Calc.: 22·25) (Found: F, 15·7. $C_4H_5O_3F$ requires F, 15·8%).

The infrared spectra were determined in CCl_4 solution, except that the semicarbazone of fluoropyruvic acid was used as a suspension in paraffin oil and fluoropyruvonitrile was investigated in chloroform solution.

The infrared spectra were kindly measured by Dr. S. Pinchas, Weizmann Institute of Science, Rehovoth.

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The Euphorbia Resins. Part IX. Corresponding Isomerisations in Tirucallol and Euphorbol.*

By J. B. Barbour, W. A. Lourens, F. L. Warren, and K. H. Watling.

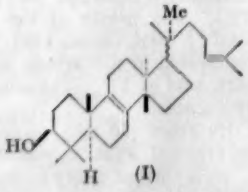
[Reprint Order No. 6014.]

Tirucallenyl and euphorbenyl acetates are isomerised to *iso*tirucallenyl and *iso*euphorbenyl acetate respectively. These *iso*-compounds form epoxides which give dehydro*iso*-compounds. Acid isomerisation of euphorbadienyl acetate results in the movement of both double bonds to give *iso*euphorbadienyl acetate.

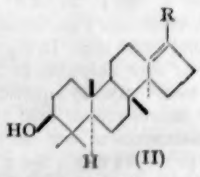
The ultraviolet extinction curves and molecular rotation differences of these compounds are compared with those reported for similar compounds from euphol.

Consideration of the data in the light of the new structure for euphol proposed by Barton, McGhie, Pradhan, and Knight (*Chem. and Ind.*, 1954, 1325; *J.*, 1955, 876) and by Arigoni, Viterbo, Dunnenberger, Jeger, and Ruzicka (*Helv. Chim. Acta*, 1954, **37**, 2306) and the identity of tirucallol and noreuphorbenol with *epi*elemenol permits complete structures for tirucallol, euphorbol, and the elemi acids to be advanced.

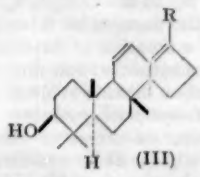
Barton, McGhie, Pradhan, and Knight (*Chem. and Ind.*, 1954, 1325) who have kindly sent us a copy of their full communication (*J.*, 1955, 876) have advanced convincing evidence for the complete structures of euphol and *iso*euphol. Arigoni, Viterbo, Dunnenberger, Jeger, and Ruzicka (*Helv. Chim. Acta*, 1954, **37**, 2306) have put forward similar structures and demonstrated that the configuration at $C_{(20)}$ is the same as in lanosterol. In addition, on the basis of a "concerted" reaction in the isomerisation of euphol to *iso*euphol they favour an α-orientation at $C_{(17)}$ for the side chain, which, however, Barton, McGhie, and their co-workers (*loc. cit.*) contend is yet unproved. The overall evidence, therefore, permits structures for euphol (I) and *iso*euphenol (II; R = $-CHMe\cdot[CH_2]_3\cdot CHMe_2$) whilst (III; R = C_8H_{17}) represents the diene prepared by Dunnenberger, Roth, Heusser, and Jeger (*Helv. Chim. Acta*, 1952, **35**, 1765) from *iso*euphenyl acetate. The configuration at $C_{(20)}$ is preserved throughout.



(I)



(II)



(III)

Arigoni, Wyler, and Jeger (*ibid.*, 1954, **37**, 1553) have corrected the formula of euphorbol to $C_{31}H_{52}O$ and identified noreuphorbenol and tirucallenol with *epi*elemenol, which has the side chain $-CHMe\cdot[CH_2]_3\cdot CHMe_2$ and is obtained from *epi*elemadienolic acid having the side chain $-CH(CO_2)\cdot[CH_2]_2\cdot CH{:}CMe_2$.

The structure of ring A for tirucallol, which follows from the experiments on ring A of the elemi acids (Halsall, Meakins, and Swayne, *J.*, 1953, 4141), is in agreement with our findings. Tirucallenol and euphorbenol with phosphorus pentachloride undergo a retropinacoline change to give *neo*tirucalladiene and *neo*euphorbadiene respectively. These *neo*-compounds with osmic acid give the corresponding glycols which with lead tetra-acetate give acetone and trisnorketones. Trisnortirucallenone resisted all attempts at crystallisation and was isolated as its 2 : 4-dinitrophenylhydrazone, m. p. 196—197°, which is different from the corresponding derivative, m. p. 143°, from euphol. The retropinacoline change in ring A results in a *cis*-indane configuration so that the difference between euphol and tirucallol, which give different trisnorketones, cannot be attributed

* Part VIII, *J.*, 1951, 2540.

solely, if at all, to a difference in A–B ring fusion. In fact euphol and euphorbol show identical bands in the infrared for their hydroxyl and acetoxyl groups, namely, at 1022 and a single maximum at 1237 cm.$^{-1}$ respectively (Cole, *J.*, 1952, 4969). In addition the small positive molecular-rotation increase on acetylation and oxidation of euphorbol and tirucallol is consistent with an equatorial configuration on an A-type terminal ring (Klyne, *J.*, 1952, 2916; cf. also Barton and Jones, *J.*, 1944, 659; Gascoigne, Robertson, and Sims, *J.*, 1953, 1833).

A difference between the lanosterol group and the euphol group has been revealed by Dawson, Halsall, and Swayne (*J.*, 1953, 590) in the molecular rotations of the 7 : 9(11)-dienes. This difference is further exemplified by the change in the molecular rotation on the formation of 7 : 11-dioxo-compounds as shown in Table 1.

TABLE 1. *Molecular rotation differences for the* 7 : 11*-dioxo-compounds.*

	A	B	C	B − A	C − A
Lanostenyl acetate	+275° [2]	+382° [1]	+275° [6]	+107°	0°
Euphenyl acetate	+165 [5]	+100 [3]	−660 [6]	− 65	−825
Tirucallenyl acetate	− 54 [3]	− 85 [7]	−656 [7]	− 31	−602
Euphorbenyl acetate	0 [3]	−200 [7]	−758 [4]	−200	−758

Column headings: A, $[M]_D$ for enyl acetate. B, $[M]_D$ for 7 : 11-dioxo-enyl acetate. C, $[M]_D$ for 7 : 11-dioxo-anyl acetate. [1] Voser, Montavon, Gunthard, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1950, **33**, 1893. [2] Ruzicka, Denss, and Jeger, *ibid.*, 1945, **28**, 759. [3] Christen, Dunnenberger, Roth, Heusser, and Jeger, *ibid.*, 1952, **35**, 1756. [4] Vogel, Jeger, and Ruzicka, *ibid.*, p. 519. [5] Newbold and Spring, *J.*, 1944, 249. [6] Dorée, McGhie, and Kurzer, *J.*, 1949, 570. [7] Haines and Warren, *J.*, 1950, 1562. [8] *Idem*, *J.*, 1949, 2554.

Additional evidence for the stereochemistry of euphol proposed by Barton, McGhie, *et al.* (*loc. cit.*) is afforded by the large decrease in the molecular rotation on the introduction of a keto-group into ring C of euphol. This indicates that ring C is of D-type (Klyne,

TABLE 2. *Rotational differences for the introduction of* 11*-keto-groups.*

	A	B	C	B − A	C − A
Lanostenyl acetate	+275°	+651° [1]	+307° [1]	+376°	+ 32°
Euphenyl acetate	+165	+139 [2]	−248 [2]	− 26	−413

Column headings: A is $[M]_D$ for the enyl acetate, *B* is $[M]_D$ for 11-oxo-Δ^9-enyl acetate, and C is $[M]_D$ for 11-oxo-anyl acetate. [1] McGhie, Pradhan, and Cavalla, *J.*, 1952, 3176. [2] Knight and McGhie, *Chem. and Ind.*, 1953, 920.

loc. cit.) which means that the 13-methyl group is α-orientated. This large decrease is also seen in the formation of the 7 : 11-dioxoeuphanyl acetate. The similar effect of the keto-groups in the molecular-rotation differences within the euphol group is indicative of a similar ring conformation.

Similarity in the rings B and C of euphol, euphorbol, and tirucallol has also been further substantiated. Dioxotirucallenyl acetate has been oxidised with selenium dioxide to trioxotirucalladienyl acetate (cf. Barbour, Bennett, and Warren, *J.*, 1951, 2540).

The evidence advanced by Barton, McGhie, *et al.* (*loc. cit.*) for the stereochemistry at $C_{(13)}$ and $C_{(14)}$ in euphol is equally applicable to tirucallol and euphorbol. The isomerisation of euphol to *iso*euphol, which finds its exact parallel in tirucallol and euphorbol, is attributed to the " conformational driving force " due to the unfavourable configuration of the C–D ring fusion. Further these workers have pointed out that the postulated stereochemistry for euphol permits an explanation of the abnormal hydrogenation of dioxoeuphenyl acetate previously reported (Barbour and Warren, *Chem. and Ind.*, 1952, 295; Knight and McGhie, *ibid.*, 1953, 920; 1954, 24). Dioxoeuphorbenyl acetate (Barbour and Warren, *loc. cit.*) and methyl acetoxy*iso*elemenadionolate (Ruzicka, Rey, Spillman, and Baumgartner, *Helv. Chim. Acta*, 1943, **26**, 1659) was also hydrogenated abnormally to αβ-unsaturated ketones.

Halsall *et al.* (*loc. cit.*) report that elemenic acid was not isomerised by chloroformic hydrogen chloride which had been used successfully by Dawson, Halsall, and Swayne (*loc. cit.*) to convert euphol into *iso*euphol. It is significant that we have found that tirucallenyl and euphorbenyl acetate are readily isomerised by sulphuric acid to *iso*tirucallenyl and *iso*euphorbenyl acetate respectively, in which the infrared spectra indicate a

tetrasubstituted double bond. The intensity values for the low-wavelength ultraviolet extinction of *iso*euphorbenyl acetate (λ 220, ε 2800; λ 223; ε 2400) and *iso*euphorbadienyl acetate (λ 220, ε 2500; λ 223, ε 1400) are consistent with a tetrasubstituted double bond exocyclic to one ring (cf. Bladon, Henbest, and Wood, *J.*, 1952, 2741) as was found by Dawson *et al.* (*loc. cit.*) for *iso*euphenyl acetate.

These *iso*-compounds gave epoxides which with sulphuric acid yielded conjugated dienes; and the ultraviolet extinction curve of dehydro*iso*euphorbenyl acetate showed maximal absorption at 247, 254, and 264 mμ (log ε 4·3, 4·33, and 4·24 respectively). This absorption is identical with that found by Dunnenberger *et al.* (*loc. cit.*) for the diene from *iso*euphenyl acetate (247, 255, and 265 mμ, log ε 4·26, 4·32, and 4·12 respectively).

The methylene group in euphorbol is assumed by Arigoni *et al.* (*loc. cit.*) to be at position 24 on biogenetic grounds. We have now established the correctness of this assumption. Isomerisation of euphorbadienyl acetate gave *iso*euphorbadienyl acetate having no strong infrared bands characteristic of a methylene link. Ozonisation of *iso*euphorbadienyl acetate gave acetone in agreement with the isomerisation $-C(:CH_2)\cdot CHMe_2 \longrightarrow -CMe{:}CMe_2$.

TABLE 3. *Molecular-rotation differences for the* iso*-compounds.*

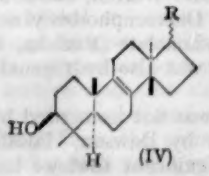
	Euphol	Tirucallol	Euphorbol
$[M]_D$ ene acetate	+193° [2]	− 79° [1]	0° [3]
$[M]_D$ *iso*ene acetate	− 47 [2]	+ 44 [4]	+ 10 [4]
$[M]_D$ dehydro*iso*ene acetate	+ 84 [3]	+267 [4]	+178 [4]
$[M]_D$ *iso*ene minus $[M_D]$ ene	−240	+123	+ 10
$[M]_D$ dehydro*iso*ene minus $[M]_D$ ene	−107	+346	+178
$[M]_D$ dehydro*iso*ene minus $[M]_D$ *iso*ene	+131	+223	+168

[1] Haines and Warren, *J.*, 1949, 2554. [2] Newbold and Spring, *J.*, 1944, 249. [3] Dawson, Halsall, and Swayne, *J.*, 1953, 590. [4] This paper.

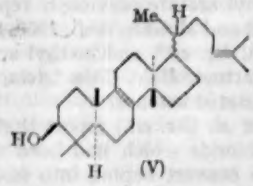
The molecular-rotation differences of derivatives of euphol, tirucallol, and euphorbol are shown in Table 3. The conversion of the *iso*enes of these three compounds into the corresponding dehydro*iso*enes results in a positive change in rotation of the same order. This is in agreement with the conclusions above that the *iso*-compounds have similar tetrasubstituted double bonds and that the dehydro*iso*-compounds have similar chromophores. The isomerisation of tirucallenyl and euphorbenyl acetate into their *iso*-compounds, however, results in a positive change in rotation whilst the formation of *iso*euphenyl acetate produces a negative change. The inert double bond in all three compounds has been placed at position 8 : 9 from the ready formation of the dioxo-enes (Haines and Warren, *J.*, 1950, 1562; Barbour, Warren, and Wood, *J.*, 1951, 2537), so that one difference between tirucallol and euphorbol on the one hand, and euphol on the other, involves the geometry of the groupings associated with the conversion of the ene into the *iso*ene.

Consideration of the above permits the partial structures put forward by Arigoni *et al.* (*loc. cit.*) to be elaborated on the basis of the formula for euphol (I).

Tiruculladienol	IV	R = $-CHMe\cdot[CH_2]_3\cdot CH{:}CMe_2$
Euphorbadienol	IV	R = $-CHMe\cdot[CH_2]_3\cdot C(:CH_2)\cdot CHMe_2$
*epi*Elemadienolic acid	IV	R = $-CH(CO_2H)\cdot[CH_2]_3\cdot CH{:}CMe_2$
*iso*Tirucallenol	II	R = $-CHMe\cdot[CH_2]_3\cdot CHMe_2$
Dehydro*iso*tirucallenol	III	
*iso*Euphorbenol	II	R = $-CHMe\cdot[CH_2]_3\cdot CHMe\cdot CHMe_2$
Dehydro*iso*euphorbenol	III	
*iso*Euphorbadienol	II	R = $-CHMe\cdot[CH_2]_3\cdot CMe{:}CMe_2$



(IV)



(V)

The group R in tirucallol and euphorbol is envisaged as having a configuration at $C_{(17)}$ opposite to that in euphol to explain one difference from euphol (I), this difference

being lost on isomerisation. *iso*Euphenol (II) and *iso*tirucallenol (II) would then differ in configuration at $C_{(20)}$. Tirucallol is accordingly (V) and is 17-*iso* : 20-*iso*euphol. It also follows that euphorbol has this same configuration at $C_{(20)}$ as in (IV). [Since this paper was presented, Arigoni, Jeger, and Ruzicka (*Helv. Chim. Acta*, 1955, **38**, 222) have advanced irrefutable evidence for the identity of the ring systems, and the difference in configuration at $C_{(20)}$, of euphol and tirucallol. Since they again favour an α-orientation of the side-chain in both these triterpenes they consider tirucallol as 20-*iso*euphol.]

The degradation of the side chain of the elemi acids was effected by Arnold, Koller, and Jeger (*Helv. Chim. Acta*, 1951, **34**, 555) and Mazur, Koller, Jeger, and Ruzicka (*ibid.*, 1952, **35**, 181) by the reactions

$$R{\cdot}CH(CO_2H){\cdot}[CH_2]_3{\cdot}CHMe_2 \longrightarrow R{\cdot}CH(CO{\cdot}N_3){\cdot}[CH_2]_3{\cdot}CHMe_2 \longrightarrow$$
$$R{\cdot}CH(NH_2){\cdot}[CH_2]_3{\cdot}CHMe_2 \longrightarrow R{\cdot}CH(NH{\cdot}CS{\cdot}NH{\cdot}C_6H_5){\cdot}[CH_2]_3{\cdot}CHMe_2 \longrightarrow$$
$$R{\cdot}CH{:}CH{\cdot}[CH_2]_2{\cdot}CHMe_2$$

The thermal elimination of the phenylthiourea gave only one product. Halsall *et al.* (*loc. cit.*) have attributed this to attachment of the side chain to the remainder of the molecule at a tertiary carbon. The formula now advanced for thee lemi acids is consistent with the non-formation of a 17 : 20-ethylenic linkage. The thermal elimination of phenylthiourea will involve a vicinal *cis*-hydrogen atom and it is unlikely that the amino-group will be able to assume a position favourable for the elimination with the 17-hydrogen atom owing to the proximity of the 13- or 14-methyl group (cf. Fieser and Fieser, *Experientia*, 1948, **4**, 286), according to the orientation at $C_{(17)}$.

Experimental.

Microanalyses are by Yvonne Merchant, ultraviolet data are by Margorie von Klemperer, and infrared data by Dr. E. C. Leisegang and A. J. Rossouw. [α] refer to chloroform solutions.

Trioxotirucalladienyl Acetate.—Dioxotirucallenyl acetate (600 mg., 1 mol.), acetic acid–acetic anhydride (1 : 1; 25 ml.), and saturated aqueous selenium dioxide (600 mg., 4·5 mols.) were refluxed for 4 hr. The ether extract, worked up in the usual way, gave a crystalline solid (600 mg.), which, dissolved in light petroleum (200 ml.), was filtered through a column of alumina (activity II; 20 g.). Light petroleum–benzene (2 : 1) eluted a yellow solid (390 mg.) which when crystallised four times from methanol gave *trioxotirucalladienyl acetate* as deep yellow plates, m. p. 183—184°, $\lambda_{max.}$ 285 mμ (log ε 3·95), infrared bands at 1659 s, 1683 s, 1709 sh., 1749, s, broad, $cm.^{-1}$. After sublimation at 150° in a high vacuum, the sample, m. p. 184—186°, was analysed (Found : C, 75·1; H, 8·9 $C_{32}H_{46}O_5$ requires C, 75·25; H, 9·1%).

neo*Euphorbadiene.*—Euphorbenol (1 g.) in light petroleum (300 ml.) was treated with phosphorus pentachloride (1 g.) at room temperature for 4 hr. whilst dry nitrogen was bubbled through the solution. The clear solution, diluted with light petroleum, washed with sodium carbonate solution, and dried (Na_2SO_4), gave a yellow solid (1 g.). A solution of this solid in light petroleum was chromatographed over alumina (activity II; 30 g.). Light petroleum eluted a colourless solid which, crystallised twice from acetone–methanol (1 : 3) and finally from acetone, gave neo*euphorbadiene* (500 mg.) as needles, m. p. 98·5—99°, $[\alpha]_D^{23}$ +15° (*c*, 1) (Found : C, 87·4; H, 12·3. $C_{31}H_{52}$ requires C, 87·7; H, 12·3%).

neo*Tirucalladiene.*—Tirucallenol (2·0 g.) was treated with phosphorus pentachloride as described above. The product, crystallised from acetone, gave neo*tirucalladiene* as needles, m. p. 107·5—108°, $[\alpha]_D^{17}$ +16·6° (*c*, 1) (Found : C, 87·8; H, 21·1. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%). When nitrogen was not passed during the reaction a chlorine-containing compound was also obtained and the yield was smaller.

neo*Euphorbenediol.*—*neo*Euphorbadiene (500 mg.) in anhydrous ether (70 ml.) was treated with osmium tetroxide (350 mg.), and the dark liquid set aside for 6 days. The product was worked up in the usual way (cf. Dorée, McGhie, and Kurzer, *J.*, 1949, 167). The benzene extract was chromatographed over alumina with light petroleum–benzene (1 : 1) to give a solid which crystallised twice from acetone–water to give neo*euphorbenediol* (300 mg.) as needles, m. p. 122—123° (Found : C, 80·8; H, 11·9. $C_{31}H_{54}O_2$ requires C, 81·1; H, 11·9%).

Oxidation of neo*Euphorbenediol.*—The diol (100 mg.), chloroform (0·5 ml.), glacial acetic acid (5 ml.), and lead tetra-acetate (0·2 g.) were set aside at room temperature overnight. The

product was treated with water and distilled. The distillate afforded acetone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 124—126°.

Formation and Oxidation of neo*Tirucallenediol.*—*neo*Tirucalladiene (1·0 g., 1 mol.) was treated with osmium tetroxide as described above, to give a very small quantity of *neo*tirucallenediol, m. p. 117—118°, which was not further purified. This was treated with lead tetra-acetate (1 mol.) as above. Water was added and a small quantity distilled into an aqueous perchloric acid solution of 2 : 4-dinitrophenylhydrazine (Neuber, Grauer, and Pisha, *Analyt. Chim. Acta*, 1952, **7**, 238) to give yellow crystals, m. p. 124°, undepressed when mixed with acetone 2 : 4-dinitrophenylhydrazone. The residue was treated with Girard's reagent P. The ketone fraction, having infrared bands at 1670 sh. and 1745 s cm.$^{-1}$, failed to crystallise and was treated with 2 : 4-dinitrophenylhydrazine. The product, crystallised from a large volume of methanol or light petroleum, gave *trisnorneotirucallenone* 2 : 4-*dinitrophenylhydrazone* in needles, m. p. 196—197° (Found : C, 70·6; H, 8·9; N, 9·9. $C_{33}H_{48}O_4N_4$ requires C, 70·2; H, 8·6; N, 9·9%).

iso*Tirucallenyl Acetate.*—Tirucallenyl acetate (2 g.) in glacial acetic acid (50 ml.) was treated with 2N-sulphuric acid (2 ml.) and refluxed for 5 hr., during which the colourless solution changed through orange to a deep purple. The product in light petroleum was chromatographed over alumina to give an oil which, crystallised three times from methanol, gave iso*tirucallenyl acetate* as laminæ, m. p. 95—96°, $[\alpha]_D^{17}$ +9·3° (*c*, 1) (Found : C, 81·7; H, 11·3. $C_{32}H_{54}O_2$ requires C, 81·6; H, 11·6%). It gave a yellow colour with tetranitromethane.

iso*Euphorbenyl Acetate.*—Euphorbenyl acetate (1·1 g.) was isomerised with dilute sulphuric acid as above. The product, crystallised from methanol, gave iso*euphorbenyl acetate*, m. p. 108—110°, $[\alpha]_D^{20}$ +2° (*c*, 1) (Found : C, 81·5; H, 11·6. $C_{32}H_{56}O_2$ requires C, 81·75; H, 11·6%).

*Epoxy*iso*tirucallanyl Acetate.*—*iso*Tirucallenyl acetate (700 mg.) with perbenzoic acid (250 mg., 1·25 mols.) in chloroform was set aside at 0°. After 29 hr. 0·91 mol. of oxygen had been absorbed and the product, worked up after 2 days, gave *epoxy*iso*tirucallanyl acetate* as a colourless gum, $[\alpha]_D^{20}$ +21·1° (*c*, 1) (Found : C, 78·8; H, 11·2. $C_{32}H_{54}O_3$ requires C, 78·9; H, 11·2%). This failed to crystallise even after chromatography and gave no colour with tetranitromethane.

*Epoxy*iso*euphorbanyl Acetate.*—*iso*Euphorbenyl acetate (0·5 g.) with perbenzoic acid in chloroform was set aside for 8 days. The product in light petroleum, filtered through alumina (grade I) and crystallised twice from methanol, gave *epoxy*iso*euphorbanyl acetate*, m. p. 60—61°, $[\alpha]_D^{20}$ −13° (*c*, 1) (Found : C, 79·3; H, 11·1. $C_{32}H_{56}O_3$ requires C, 79·1; H, 11·3%).

*Dehydro*iso*tirucallenyl Acetate.*—Epoxyisotirucallanyl acetate (400 mg.) in acetic acid (58 ml.) was treated with concentrated sulphuric acid (six drops) and heated for 2 hr. on a water-bath. The product, crystallised four times from methanol, gave *dehydro*iso*tirucallenyl acetate* as rhombohedra, m. p. 85°, $[\alpha]_D^{21}$ +57° (*c*, 1), $\lambda_{max.}$ 250 mμ (log ε 3·80 in EtOH) (Found : C, 82·1; H, 11·2. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%).

*Dehydro*iso*euphorbenyl Acetate*—Epoxyisoeuphorbanyl acetate (200 mg.), glacial acetic acid (20 c.c.), and concentrated sulphuric acid (3 drops) were set aside overnight at room temperature. The product in light petroleum was chromatographed over alumina. The first fraction gave a waxy solid which, crystallised from methanol, gave *dehydro*iso*euphorbenyl acetate* as laminæ, m. p. 106·5—107°, $[\alpha]_D^{22}$ +37° (*c*, 1) (Found : C, 82·2; H, 11·3. $C_{32}H_{54}O_2$ requires C, 82·1; H, 11·3%). The crystals showed in alcohol absorption max. at 247, 254, 264 mμ (log ε 4·3, 4·33, 4·24 respectively) and were coloured dark brown with tetranitromethane.

iso*Euphorbadienyl Acetate.*—Euphorbadienyl acetate (1 g.), glacial acetic acid, and 2N-sulphuric acid were refluxed and worked up as above. The product, crystallised three times from acetone, gave iso*euphorbadienyl acetate* as needles, m. p. 129—130°, $[\alpha]_D^{20}$ 0° (*c*, 1) (Found : C, 82·0; H, 11·2. $C_{32}H_{54}O_2$ requires C, 82·1; H, 11·3%). Ozonolysis of this product gave acetone characterised as its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 120—122°.

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β-Aroylpropionic Acids. Part V. The Synthesis of β-Aroyl-α-methylpropionic Acids, and their Conversion into Polynuclear Compounds.*

By F. G. Baddar, Hussein A. Fahim, and Abdallah M. Fleifel.

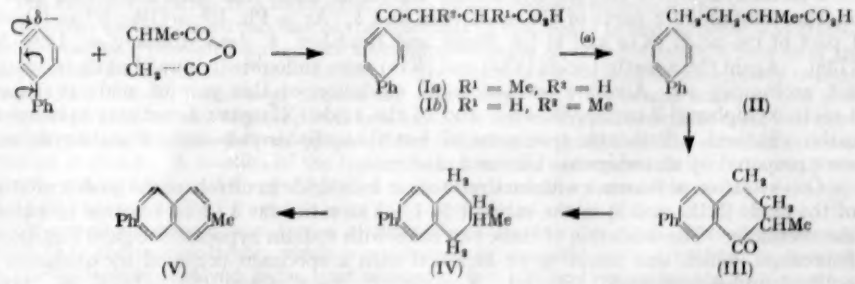
[Reprint Order No. 6095.]

4 : 4′- and 2 : 2′-Dimethoxydiphenyl condense with succinic anhydride in presence of aluminium chloride to give β-2-methoxy-5-*p*-methoxyphenyl- and β-4-methoxy-3-*o*-methoxyphenyl-benzoylpropionic acid, respectively. Condensation of diphenyl and the above derivatives with methylsuccinic anhydride gives two products in each case, Ar·CO·CH_2·CHMe·CO_2H and Ar·CO·CHMe·CH_2·CO_2H. Two acids of the former type are cyclised to naphthalene derivatives. 4-Methoxydiphenyl gives four products, two of each type.

Fluorene gives similarly a product of each type, and the α-methyl acid is converted into 3′-methyl-2 : 3-benzofluorene.

Several investigators have reported that condensed polynuclear compounds such as naphthalene (Haworth, *J.*, 1932, 1125), phenanthrene (Cook and Haslewood, *J.*, 1934, 428; Bergmann and Blum-Bergmann, *J. Amer. Chem. Soc.*, 1937, **59**, 1573), α- and β-methylnaphthalene (Haworth, Melvin, and Sheldrick, *J.*, 1934, 454; and Haworth and Bolam, *J.*, 1932, 2248, respectively), and some phenolic ethers such as anisole and *o*-, *m*-, and *p*-tolyl methyl ether, condense with methylsuccinic anhydride in presence of aluminium chloride to give only the β-aroyl-α-methylpropionic acid. We have studied in this investigation whether this is true for diphenyl and some of its derivatives and fluorene. The products were always mixtures of the α- and the β-methyl acid, Ar·CO·CH_2·CHMe·CO_2H and Ar·CO·CHMe·CH_2·CO_2H, in which the former predominated. The structures of the α-methyl acids were deduced from the facts that they were the less soluble isomers (*Org. Reactions*, 1949, **5**, 243) and with an alcoholic solution of salicylaldehyde and dry hydrogen chloride gave precipitates of the coloured pyrylium derivatives (cf. Mitter and De, *J. Indian Chem. Soc.*, 1939, **16**, 199; Desai and Wali, *Proc. Indian Acad. Sci.*, 1937, **6**, *A*, 135). The other isomers failed to give this reaction.

Thus, diphenyl and methylsuccinic anhydride in nitrobenzene gave a mixture of the acids (I*a* and *b*) in the ratio of 12 : 1. The yield of the latter acid increased when nitrobenzene was replaced by *s*-tetrachloroethane. The position of attack on the diphenyl nucleus was elucidated by oxidising both acids to diphenyl-4-carboxylic acid.



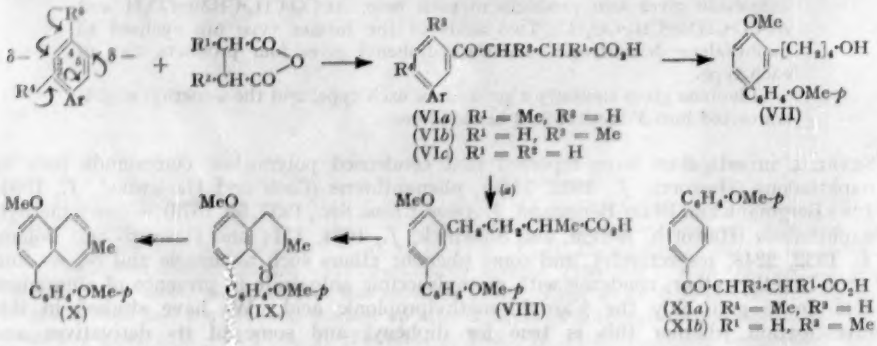
The α-methyl-keto-acid (I*a*) was reduced by Clemmensen's method to the butyric acid (II), which was cyclised with phosphoric oxide to the tetralone (III). This was reduced by lithium aluminium hydride to the tetralin (IV), which was dehydrogenated with selenium to 2-methyl-7-phenylnaphthalene (V).

4 : 4′- and 2 : 2′-Dimethoxydiphenyl condensed with succinic anhydride to give the acids (VI*c*; Ar = *p*-MeO·C_6H_4, R^3 = OMe, R^4 = H) and (VI*c*; Ar = *o*-MeO·C_6H_4, R^3 = H,

* Part IV, *J.*, 1955, 453.

R^4 = OMe), respectively, which were oxidised to 2-methoxy-5-*p*-methoxy- and 4-methoxy-3-*o*-methoxy-phenylbenzoic acid, respectively. Authentic specimens of the benzoic acids were prepared by condensing methyl 5-bromo-2-methoxybenzoate with *p*-iodoanisole and methyl 3-iodo-4-methoxybenzoate with *o*-iodoanisole in presence of copper bronze. This showed that electrophilic substitution in the 4 : 4′- and 2 : 2′-dimethoxydiphenyl molecules takes place at positions 3 and 5, respectively.

Attempted reduction of the acid (VI*c*; Ar = *p*-MeO·C_6H_4, R^3 = MeO, R^4 = H) by the Clemmensen method or its modifications was unsuccessful. Its reduction with excess of lithium aluminium hydride gave the butanol (VII), which gave a resin on attempted cyclisation with phosphoric oxide. With methylsuccinic anhydride 4 : 4′-dimethoxydi-



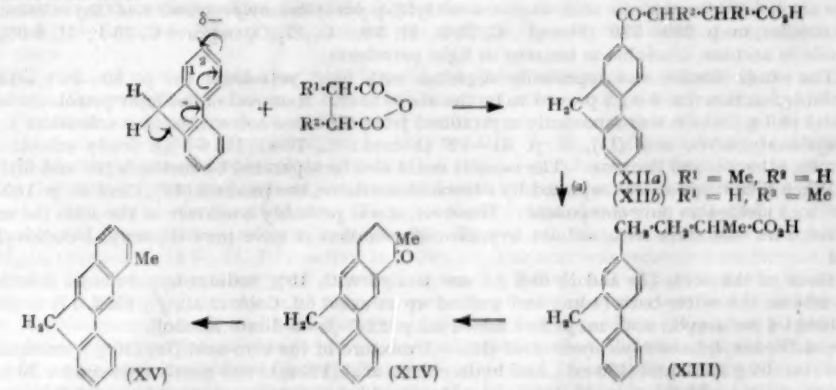
phenyl gave a mixture of the acids (VI*a* and *b*; Ar = *p*-MeO·C_6H_4, R^3 = OMe, R^4 = H), and 2 : 2′-dimethoxydiphenyl gave a corresponding pair (Ar = *o*-MeO·C_6H_4). The structures were established by the pyrylium reaction and by oxidising the first pair of acids to 2-methoxy-5-*p*-methoxyphenyl- and the latter pair to 4-methoxy-3-*o*-methoxyphenyl-benzoic acid, but the acids (VI*b*) were rather indefinite materials and may not have been pure isomers. The α-methyl-keto-acid (VI*a*; Ar = *p*-MeO·C_6H_4, R^3 = OMe, R^4 = H) was reduced by Clemmensen's method to the butyric acid (VIII), which was cyclised to the tetralone (IX). This was converted into 1-methoxy-4-*p*-methoxyphenyl-6-methyl-naphthalene (X) by reduction with lithium aluminium hydride followed by dehydrogenation with selenium.

4-Methoxydiphenyl and methylsuccinic anhydride under the same conditions gave a mixture containing 2 parts of the acids (VI*a* and *b*; Ar = Ph, R^3 = OMe, R^4 = H) and 1 part of the acids (XI*a* and *b*) (cf. Fieser and Bradsher, *J. Amer. Chem. Soc.*, 1936, **58**, 1738). Again the α-methyl acids (VI*a*) and (XI*a*) were undoubtedly pure, but their isomers not necessarily so. Alkaline permanganate oxidation of this pair of acids (VI) gave 4-methoxydiphenyl-3-carboxylic acid, and of the acids (XI) gave 4-methoxydiphenyl-4′-carboxylic acid. Authentic specimens of 4-methoxydiphenyl-3- and -4′-carboxylic acid were prepared by unambiguous Ullmann reactions.

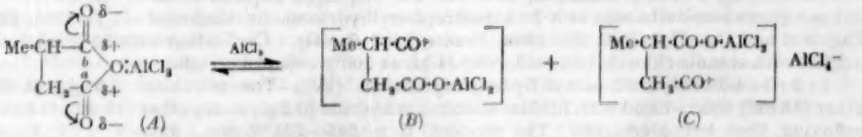
Condensation of fluorene with methylsuccinic anhydride in nitrobenzene gave a mixture of the acids (XII*a* and *b*) in the ratio of 5 : 1. The ratio was 3 : 1 on reaction in *s*-tetrachloroethane. The oxidation of these two acids with sodium hypobromite gave 2-carboxyfluorenone, which was found to be identical with a specimen prepared by oxidation of γ-2-fluorenyl-γ-oxobutyric acid (cf. Koelsch, *J. Amer. Chem. Soc.*, 1933, **55**, 3885). Reduction of the α-methyl-keto-acid (XII*a*) by Clemmensen's method gave γ-2-fluorenyl-α-methylbutyric acid (XIII). Cyclisation of the butyric acid with phosphorus oxychloride in *s*-tetrachloroethane gave the oxobenzofluorene (XIV), converted into 3′-methyl-2 : 3-benzofluorene (XV) on reduction with lithium aluminium hydride followed by dehydrogenation with sulphur. The assignment of a 2 : 3- and not a 1 : 2-benzofluorene structure to the product was based on analogy with γ-2-fluorenylbutyric acid (cf. Koelsch, *loc. cit.*).

The preferential substitution of fluorene by electrophilic reagents at position 2 indicates

that this carbon atom carries the highest electron density, owing to the electronic displacements indicated.



The above results, as well as unpublished results on anisole and toluene, showed that the amount of the β-methyl-keto-acid (β-aroylbutyric acid) increased with the decrease in the dielectric constant of the medium. This may be due to the fact that in this case the complex (*A*) rather than (*B*) and (*C*) (cf. Groggins and Nagel, *Ind. Eng. Chem.*, 1934, **26**, 1313; Saboor, *J.*, 1945, 922) is the main constituent of the mixture. The ratio of the



α- to the β-methyl-keto-acid will be directly proportional to the electron deficiencies at carbon atoms (*a*) and (*b*), respectively. In solvents with high dielectric constant such as nitrobenzene, ion (*C*) is the main constituent of the mixture, thus leading predominantly to the α-methyl-keto-acid.

Experimental

The Friedel–Crafts reaction was carried out as follows unless otherwise stated.

A stirred and ice-cooled mixture of the reactants (1 mol. each) in nitrobenzene was treated portionwise with powdered anhydrous aluminium chloride (2 mols.) at such a rate that the temperature did not exceed 5° (30—45 min.). The mixture was allowed to come slowly to room temperature (20—30°) and kept thereat for a few days with occasional stirring, and then decomposed with ice and dilute hydrochloric acid. When methylsuccinic anhydride was used, the isomeric acids were separated by one of the following methods. (*i*) The nitrobenzene was removed in steam. A solution of the residue in hot sodium carbonate solution (charcoal) was filtered, and acidified, and the precipitated acids were worked up according to (*a*) and/or (*b*): (*a*) They were crystallised from the least amount of glacial acetic acid or ethyl alcohol: the β-aroyl-α-methylpropionic acid (series *a*) crystallised, leaving the crude β-aroylbutyric acid (series *b*) in the mother-liquor, which was obtained by evaporation in a vacuum to dryness. (*b*) The acids were dissolved in the least amount of hot 10% sodium carbonate solution, then cooled in ice, and the precipitated sodium salt was decomposed with hot dilute hydrochloric acid to give the α-methylpropionic acid; the sodium carbonate mother-liquor gave the crude isomer on acidification. (*ii*) The insoluble α-methylpropionic acid was filtered off; the nitrobenzene solution was extracted with ammonia solution, which gave on acidification the crude β-aroylbutyric acid (cf. Cocker *et al.*, *J.*, 1951, 926).

Diphenyl and Methylsuccinic Anhydride.—The mixture from methylsuccinic anhydride (cf. *Org. Synth.*, 1946, **26**, 54; Dev and Guha, *J. Indian Chem. Soc.*, 1948, **25**, 13) (8·4 g.), diphenyl (10 g.), nitrobenzene (80 ml.), and aluminium chloride (17·8 g.) (5 days) was worked up

according to method (*ia*). The product (15 g., 86%), m. p. 190—202°, was crystallised from the least amount of ethyl alcohol (*ca.* 380 ml.). The crystalline acid (7·1 g.) was recrystallised from alcohol or glacial acetic acid, to give *α-methyl-β-p-phenylbenzoylpropionic acid* (I*a*) in colourless needles, m. p. 209—210° (Found: C, 75·5; H, 5·9. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%), soluble in acetone, insoluble in benzene or light petroleum.

The crude isomer was repeatedly digested with light petroleum (b. p. 50—60°). The insoluble fraction (*ca.* 1·0 g.) proved to be the above acid. Removal of the light petroleum left a solid (0·7 g.) which was repeatedly crystallised from the same solvent, to give colourless *β-p-phenylbenzoylbutyric acid* (I*b*), m. p. 81—82° (Found: C, 76·4; H, 6·3%), freely soluble in acetone, ethanol, and benzene. The isomers could also be separated by methods (*ib*) and (ii).

When nitrobenzene was replaced by *s*-tetrachloroethane, the product (60%) had m. p. 160—170°, and yielded no pure component. However, it was probably a mixture of the acids (I*a* and *b*), since on oxidation with sodium hypobromite solution it gave pure diphenyl-4-carboxylic acid.

Each of the acids (I*a* and *b*) (0·4 g.) was heated with 10% sodium hypobromite solution (45 ml.) on the water-bath (4 hr.) and worked up as usual (cf. Cook *et al.*, *J.*, 1953, 11) to give diphenyl-4-carboxylic acid, m. p. and mixed m. p. 224° (from dilute alcohol).

γ-4-Diphenylyl-α-methylbutyric Acid (II).—A mixture of the keto-acid (I*a*) (20 g.), amalgamated zinc (50 g.), ethanol (120 ml.), and hydrochloric acid (120 ml.) was gently refluxed for 30 hr., during which hydrochloric acid (total, 80 ml.) was added in portions every 6 hr. *γ-4-Diphenylyl-α-methylbutyric acid* (90%) was obtained in colourless needles, m. p. 90—91° [from light petroleum (b. p. 50—60°)] (Found: 79·7; H, 6·9. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%).

2-Methyl-7-phenyl-1-tetralone (III).—The butyric acid (5 g.) was refluxed with phosphoric oxide (28·5 g.) in dry benzene (60 ml.) for 3·5 hr., the oxide being added portionwise. The product was worked up as usual and distilled, to give *2-methyl-7-phenyl-1-tetralone* (64%), b. p. 178—180°/6 mm., n_D^{25} 1·6980 (Found: C, 85·8; H, 6·5. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8%). It did not give a semicarbazone or a 2 : 4-dinitrophenylhydrazone (cf. Cocker *et al.*, *J.*, 1951, 926; Cagniant and Buu-Hoï, *Bull. Soc. chim. France*, 1942, **9**, 841). Cyclisation with 85% sulphuric acid or with stannic chloride (acid chloride) (4 hr. at 100°) was unsuccessful.

1 : 2 : 3 : 4-*Tetrahydro-2-methyl-7-phenylnaphthalene* (IV).—The tetralone (0·5 g.) in dry ether (15 ml.) was reduced with lithium aluminium hydride (0·2 g.) in dry ether (15 ml.) (3 hours' refluxing, then left overnight). The product, b. p. 225—235°/6 mm., gave 1 : 2 : 3 : 4-*tetrahydro-2-methyl-7-phenylnaphthalene* (64%) in colourless needles [from light petroleum (b. p. <40°)], m. p. 39—40° (Found: C, 91·2; H, 8·2. $C_{17}H_{18}$ requires C, 91·9; H, 8·1%). The tetralone was recovered unchanged after treatment by Clemmensen's method or its modifications.

2-Methyl-7-phenylnaphthalene (V).—The tetrahydronaphthalene (0·5 g.) was heated with selenium (0·6 g.) at 330—340° for 2·5 hr. The product was extracted with ether, to give *2-methyl-7-phenylnaphthalene* (40%), m. p. 141—142° [from light petroleum (b. p. 50—60°)] (Found: C, 92·8; H, 6·2. $C_{17}H_{14}$ requires C, 93·5; H, 6·5%).

Diphenyl-4-carboxylic Acid.—Copper bronze (3·8 g.) was added portionwise during ½ hr. to a stirred mixture of methyl *p*-iodobenzoate (2·6 g., 1 mol.) and iodobenzene (2 g., 1 mol.) at 170°. The temperature was kept thereat for a further ½ hr., then gradually raised to 230—235°. More iodobenzene (4 g.) was added in two portions at hourly intervals, then the heating was continued for further 2 hr. The product was worked up as stated by Baddar and Gindy (*J.*, 1948, 1231). The acid soluble in benzene was converted into its methyl ester, b. p. 220—230°/18 mm., then hydrolysed with alcoholic sodium hydroxide to diphenyl-4-carboxylic acid (0·8 g., 40%), m. p. 226—227° (from dilute alcohol) (Found: C, 78·3; H, 5·0. Calc. for $C_{13}H_{10}O_2$: C, 78·75; H, 5·1%). Liebermann and Zsuffa (*Ber.*, 1911, **44**, 852) and Gull and Turner (*J.*, 1929, 498) gave m. p. 224° and 228°, respectively. The benzene-insoluble acid, m. p. >300°, was esterified (methyl alcohol and sulphuric acid, 5 hr.) to give dimethyl diphenyl-4 : 4′-dicarboxylate, m. p. and mixed m. p. 211—212° (from methyl alcohol) (Found: C, 71·3; H, 5·3. Calc. for $C_{16}H_{14}O_4$: C, 71·1; H, 5·2%). Weiler (*Ber.*, 1899, **32**, 1063) and Ullmann *et al.* (*Annalen*, 1904, **332**, 73) gave m. p. 212—213° and 214°, respectively.

4 : 4′-Dimethoxydiphenyl and Succinic Anhydride.—A stirred mixture of 4 : 4′-dimethoxydiphenyl (10 g.), aluminium chloride (13·4 g.), and nitrobenzene (50 ml.) was treated portionwise with a solution of succinic anhydride (5·2 g.) in nitrobenzene (200 ml.), then left overnight. The product was decomposed with ice and hydrochloric acid and treated with benzene, and the organic layer was extracted with sodium carbonate solution (charcoal), which was later acidified. The precipitated acid (14·6 g.; m. p. 123—125°) was *β-2-methoxy-5-p-methoxyphenylbenzoylpropionic acid* (VI*c*; Ar = *p*-MeO·C_6H_4, R^3 = OMe, R^4 = H), colourless crystals (from benzene),

m. p. 135—136° (Found: C, 68·5; H, 5·8; OMe, 19·5. $C_{19}H_{18}O_5$ requires C, 68·8; H, 5·8; OMe, 19·7%), soluble in ethanol or acetone, and insoluble in ether and light petroleum. When the reaction was carried out as described in the first experiment, an uncrystallisable sticky material was obtained. When nitrobenzene was replaced by *s*-tetrachloroethane no reaction took place.

This acid (0·4 g.) was oxidised with 10% sodium hypobromite solution (45 ml.) in the usual manner. The precipitated acid, m. p. 133—135°, was converted into its methyl ester, m. p. 80—81° [from light petroleum (b. p. 50—60°)], undepressed on admixture with methyl 2-methoxy-5-*p*-methoxyphenylbenzoate (Found: C, 70·4; H, 5·9. Calc. for $C_{16}H_{16}O_4$: C, 70·6; H, 5·9%).

4-(2-*Methoxy*-5-p-*methoxyphenylphenyl*)*butan*-1-*ol* (VII).—A solution of the keto-acid (5 g.) in dry thiophen-free benzene (100 ml.) was reduced with lithium aluminium hydride (2·5 g.) in dry ether (200 ml.) as mentioned above. The *alcohol* (66%) was obtained in colourless needles, m. p. 67—68°, from light petroleum (b. p. 50—60°) (Found: C, 75·4; H, 7·5; active H, 0·35. $C_{18}H_{22}O_3$ requires C, 75·5; H, 7·7; active H, 0·35%). The acid was recovered unchanged on treatment by Clemmensen's method. Attempts to cyclise this alcohol with phosphoric oxide in benzene on a boiling-water bath or at room temperature gave viscous uncrystallisable material.

4 : 4′-*Dimethoxydiphenyl and Methylsuccinic Anhydride*.—The product (15 g.; m. p. 142—150°) from 4 : 4′-dimethoxydiphenyl (10 g.), methylsuccinic anhydride (5·8 g.), nitrobenzene (80 ml.), and aluminium chloride (13 g.) (3 days) was worked up according to procedure (*ia*). β-(2-*Methoxy*-5-p-*methoxyphenylbenzoyl*)-α-*methylpropionic acid* (VI*a*; Ar = *p*-MeO·C_6H_4, R^3 = OMe, R^4 = H) (9·0 g. from 20 ml. of glacial acetic acid) was obtained in colourless needles, m. p. 159—160° (Found: C, 68·9; H, 5·8; OMe, 18·4. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·1; OMe, 18·9%). The crude isomer (4 g.) failed to solidify. It was repeatedly extracted with boiling light petroleum (b. p. <40°), and the combined extracts were concentrated and kept in the ice-chest (one month) to give the aroylbutyric acid as a pale yellow solid, m. p. 80—100° not improved by recrystallisation. It failed to give a solid semicarbazone or a 2 : 4-dinitrophenylhydrazone. Both acids gave on oxidation with sodium hypobromite solution 2-methoxy-5-methoxyphenylbenzoic acid. The acids could also be separated by method (ii).

γ-(2-*Methoxy*-5-p-*methoxyphenylphenyl*)-α-*methylbutyric Acid* (VIII).—The keto-acid (7 g.) was reduced with zinc amalgam (25 g.) and hydrochloric acid (100 ml.) (20 hr.) to this *butyric acid* (89%), colourless needles [from light petroleum (b. p. 100—120°)], m. p. 119—120° (Found: C, 72·6; H, 6·9; OMe, 19·1. $C_{19}H_{22}O_4$ requires C, 72·6; H, 7·1; OMe, 19·7%).

5-*Methoxy*-8-p-*methoxyphenyl*-2-*methyl*-1-*tetralone* (IX).—A benzene solution of the acid chloride of the above butyric acid (6·4 g.) [prepared by phosphorus pentachloride (4 g.)] was cooled in ice, treated dropwise during 15 min. with a solution of stannic chloride (3 ml.) in dry thiophen-free benzene (10 ml.), left overnight, and worked up as usual. The *tetralone* (60%) was obtained in pale yellow crystals [from light petroleum (b. p. 100—120°)], m. p. 140—141° (Found: C, 76·6; H, 6·9. $C_{19}H_{20}O_3$ requires C, 77·0; H, 6·8%).

1 : 2 : 3 : 4-*Tetrahydro*-5-*methoxy*-8-p-*methoxyphenyl*-2-*methylnaphthalene*.—A solution of the above tetralone (1 g.) in dry ether (20 ml.) and dry thiophen-free benzene (20 ml.) was reduced with lithium aluminium hydride (0·5 g.) in dry ether (15 ml.) (2 hours' refluxing), then worked up as usual. The product, b. p. 225—235°/7 mm. (75%), gave the *tetrahydronaphthalene*, m. p. 84—85° (from alcohol) (Found: C, 81·0; H, 7·6. $C_{19}H_{22}O_2$ requires C, 80·8; H, 7·9%). The substance contained no active hydrogen, which proved that it was a tetralin.

1-*Methoxy*-4-p-*methoxyphenyl*-6-*methylnaphthalene* (X).—The tetrahydronaphthalene (0·5 g.) was heated with selenium (0·5 g.) at 330—340° for 2 hr. 1-*Methoxy*-4-p-*methoxyphenyl*-6-*methylnaphthalene* (40%) was obtained nearly colourless (from alcohol), m. p. 126—127° (Found: C, 81·3; H, 6·5; MeO, 22·5. $C_{19}H_{18}O_2$ requires C, 82·0; H, 6·5; MeO, 22·3%).

5-*Bromo*-2-*methoxybenzoic Acid*.—2-Methoxybenzoic acid (5 g.) was treated with bromine in the manner adopted by Derbyshire and Waters (*J.*, 1950, 576) for benzoic acid (2 hr. at room temperature). The product (98%), m. p. 119°, was pure enough for the next step (Peratoner, *Gazzetta*, 1886, **16**, 405, gave the same m. p.). The methyl ester had m. p. 39—40°. Peratoner (*loc. cit.*) gave the same m. p.

Methyl 2-*Methoxy*-5-p-*methoxyphenylbenzoate*.—A stirred mixture of the above ester (4 g., 1 mol.) and *p*-iodoanisole (3·7 g., 1 mol.) was treated portionwise at 180° with copper bronze (5·1 g.). The temperature was then raised to 230—235° and maintained thereat for 6 hr., and the product worked up as usual. The acid soluble in benzene was esterified, to give *methyl* 2-*methoxy*-5-p-*methoxyphenylbenzoate*, b. p. 230—240°/6 mm. (7%), needles [from light petroleum (b. p. 50—60°)], m. p. 80—81° (Found: C, 70·3; H, 5·8; OMe, 34·5. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9; OMe, 34·2%).

2 : 2′-*Dimethoxydiphenyl and Succinic Anhydride.*—The product (14 g.; m. p. 223—225°) from 2 : 2′-dimethoxydiphenyl (10 g.), succinic anhydride (5·2 g.), nitrobenzene (80 ml.), and aluminium chloride (13·6 g.) (2 days) gave β-(4-*methoxy*-3-*o*-*methoxyphenylbenzoyl*)*propionic acid*, colourless needles (from acetic acid), m. p. 229—230° (darkened at 200°) (Found: C, 64·1; H, 5·8; OMe, 17·1. $C_{18}H_{18}O_6,CH_3{\cdot}CO_2H$ requires C, 64·1; H, 5·9; MeO, 16·6%). The proof of the presence of acetic acid of crystallisation rested entirely on the analysis. The acid could also be purified through its insoluble sodium salt. Its *ethyl ester* had m. p. 152—153° (from ethanol) (Found: 69·7; H, 6·4. $C_{20}H_{22}O_5$ requires C, 70·1; H, 6·5%). Attempts to reduce this keto-acid or its ester by the Clemmensen method or its modifications were not successful. Lithium aluminium hydride gave a neutral oil which failed to give a solid toluene-*p*-sulphonate or a 3 : 5-dinitrobenzoate. The keto-acid, on oxidation with 10% sodium hypobromite solution, gave 4-methoxy-3-*o*-methoxyphenylbenzoic acid, m. p. 334—336° (from acetic acid). Its methyl ester, stout monoclinic crystals (from methanol), had m. p. and mixed m. p. 171—172°.

Methyl 4-*Methoxy*-3-*o*-*methoxyphenylbenzoate.*—The reaction between methyl 3-iodo-4-methoxybenzoate (3·5 g.), copper bronze (4 g.), and *o*-iodoanisole (2·8 g.) was complete in 4 hr. (230—235°). The product was worked up as usual, and the neutral fraction proved to be 2 : 2′-dimethoxydiphenyl. 4-Methoxy-3-*o*-methoxyphenylbenzoic acid, needles (from acetic acid), m. p. 330—336°, gave a methyl *ester* (13%), monoclinic crystals, m. p. 171—172°, from methanol (Found: C, 69·9; H, 5·6; OMe, 33·4. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9; OMe, 34·2%).

2 : 2′-*Dimethoxydiphenyl and Methylsuccinic Anhydride.*—The product (m. p. 200—211°; 15 g.) from 2 : 2′-dimethoxydiphenyl (10 g.), methylsuccinic anhydride (5·8 g.), nitrobenzene (80 ml.), and aluminium chloride (13 g.) was worked up according to method (1; *a*). β-(4-*Methoxy*-3-*o*-*methoxyphenylbenzoyl*)-α-*methylpropionic acid* (8 g.; from 20 ml. of glacial acetic acid) was obtained in colourless needles, m. p. 234—235° (Found: C, 65·0; H, 5·9; OMe, 15·2. $C_{19}H_{20}O_6,CH_3{\cdot}CO_2H$ requires C, 64·9; H, 6·2; OMe, 16·0%). The product in the acetic acid mother-liquor failed to solidify or to give a semicarbazone or 2 : 4-dinitrophenylhydrazone. However, it was most probably the β-aroylbutyric acid. Both the keto-acids, on oxidation with sodium hypobromite solution and esterification, gave methyl 4-methoxy-3-*o*-methoxyphenylbenzoate, m. p. and mixed m. p. 171—172°. Attempted reduction of the α-methyl acid by Clemmensen's method was unsuccessful (cf. Cook *et al.*, *loc. cit.*). Reduction with lithium aluminium hydride gave a neutral oil from which no solid toluene-*p*-sulphonate or 3 : 5-dinitrobenzoate could be obtained.

Methylsuccinic Anhydride and 4-*Methoxydiphenyl.*—The product (23 g.; m. p. 120—162°) from aluminium chloride (21 g.), 4-methoxydiphenyl (15 g.), methylsuccinic anhydride (10·2 g.), and nitrobenzene (120 ml.) (overnight) was worked according to (*ib*). The acids (7 g.) resulting from the acidification of the insoluble sodium salts had m. p. 180—202° and on repeated crystallisation from glacial acetic acid (*ca.* 40 ml.) gave β-4-p-*methoxyphenylbenzoyl*-α-*methylpropionic acid* (3·4 g.), m. p. 204—205° (Found: C, 72·7; H, 6·3; OMe, 11·3. $C_{18}H_{18}O_4$ requires C, 72·45; H, 6·1; OMe, 10·4%). The first acetic acid mother-liquor was evaporated in a vacuum to dryness, and the residue (*ca.* 2 g.) was triturated with light petroleum (b. p. <40°). It melted at 147—165° (shrinking at 140°), and the m. p. was not improved by repeated crystallisation. It was probably impure β-4-*p*-methoxyphenylbenzoylbutyric acid. Both the keto-acids on oxidation with alkaline permanganate (cf. Fieser and Bradsher, *J. Amer. Chem. Soc.*, 1936, **58**, 1738) gave 4′-methoxydiphenyl-4-carboxylic acid, m. p. and mixed m. p. 248—249°. The acids liberated from the soluble sodium salts gave β-(2-*methoxy*-5-*phenylbenzoyl*)-α-*methylpropionic acid* (*ca.* 7 g.; m. p. 132—134°), m. p. 146—147° [repeatedly crystallised from benzene–light petroleum (b. p. 50—60°)] (Found: C, 72·2; H, 5·9; OMe, 12·2. $C_{18}H_{18}O_4$ requires C, 72·45; H, 6·1; OMe, 10·4%). The benzene–light petroleum mother-liquor left on evaporation an oil (*ca.* 3 g.), which was triturated with light petroleum (b. p. <40°), then crystallised from benzene–light petroleum (b. p. 50—60°) to give impure β-2-methoxy-5-phenylbenzoylbutyric acid, m. p. 105—120°. The m. p. did not improve by repeated crystallisation from the same solvent. Both acids on oxidation with alkaline permanganate gave 4-methoxydiphenyl-3-carboxylic acid, m. p. and mixed m. p. 169—170° (Fieser and Bradsher, *loc. cit.*, gave m. p. 166—167°). Oxidation of these keto-acids with alkaline hypobromite gave unsatisfactory results.

4′-*Methoxydiphenyl*-4-*carboxylic Acid.*—This was prepared from methyl *p*-iodobenzoate (7·8 g.), *p*-iodoanisole (6·9 g.), and copper bronze (11·4 g.) in the usual manner (5 hr. at 230—235°). The benzene-soluble acid (0·6 g., 9%) gave 4′-methoxydiphenyl-4-carboxylic acid, needles (from acetic acid), m. p. 248—249° (Found: C, 72·6; H, 5·1; OMe, 15·2. Calc. for $C_{14}H_{12}O_3$: C, 73·6; H, 5·3; OMe, 13·6%). Fieser and Bradsher (*loc. cit.*) gave the same m. p. The

benzene-insoluble acid on methylation gave dimethyl diphenyl-4 : 4′-dicarboxylate, m. p. and mixed m. p. 211—212° (from methanol).

4-*Methoxydiphenyl-3-carboxylic Acid.*—This was prepared from methyl 5-bromo-2-methoxybenzoate (4·9 g., 1 mol.), iodobenzene (12·3 g., 3 mols.), and copper bronze (7·6 g.) in the usual manner (5 hr. at 230—235°). The iodobenzene was added in portions during the first 2 hr. The benzene-soluble acid (0·5 g., 11%) gave 4-methoxydiphenyl-3-carboxylic acid, m. p. 159—170° (from ether) (Found : C, 72·9; H, 5·2; OMe, 14·6. Calc. for $C_{14}H_{12}O_3$: C, 73·6; H, 5·3; OMe, 13·6%). Fieser and Bradsher (*loc. cit.*) gave m. p. 166—167°.

Fluorene and Methylsuccinic Anhydride.—The product from fluorene (10 g.), methylsuccinic anhydride (8·2 g.), nitrobenzene (80 ml.), and aluminium chloride (19 g.) (3 days) was worked up according to procedure (ii). The insoluble acid (14 g.; m. p. 204—206°) gave *γ-2-fluorenyl-α-methyl-γ-oxobutyric acid* (XII*a*), needles, m. p. 212—213° (from acetic acid) (Found : C, 77·2; H, 5·8. $C_{18}H_{16}O_3$ requires C, 77·1; H, 5·8%). It was soluble in ethanol, insoluble in benzene. The pale yellow acid (2 g.), recovered from the ammonia, gave *β-(2-fluorenylcarbonyl)butyric acid* (XII*b*), m. p. 113—116° [from light petroleum, b. p. 100—120°)] (Found : C, 76·6; H, 5·7%).

The crude acids were also separated by procedure (1; *b*) in the ratio of 5 : 1. When nitrobenzene was replaced by *s*-tetrachloroethane, the ratio of the acids, separated by procedure (*ib*), was 3 : 1. Both acids on oxidation with sodium hypobromite solution gave an acid, the methyl ester of which was identical with methyl fluorenone-2-carboxylate. This was prepared by the oxidation of *γ*-2-fluorenyl-*γ*-oxobutyric acid (cf. Koelsch, *J. Amer. Chem. Soc.*, 1933, **55**, 3885) with alkaline hypobromite, followed by methylation, and had m. p. and mixed m. p., 179—180°. Fortner (*Monatsh.*, 1904, **25**, 443) and Koelsch (*loc. cit.*) gave m. p. 181° and 177—181°, respectively.

γ-2-Fluorenyl-α-methylbutyric Acid (XIII).—The keto-acid (XII*a*) (20 g.) was reduced with zinc amalgam (100 g.), ethanol (150 ml.), and hydrochloric acid (250 ml.) (30 hours' refluxing) in the usual manner. *γ-2-Fluorenyl-α-methylbutyric acid* (17 g.) was obtained in colourless needles, m. p. 124—125° [from light petroleum (b. p. 100—120°)] (Found : C, 81·4; H, 7·0. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8%).

1′ : 2′ : 3′ : 4′-*Tetrahydro-3′-methyl-4′-oxo-2* : 3-*benzofluorene* (XIV).—The butyric acid (1·5 g.) was cyclised with phosphorus oxychloride (1·5 ml.) in dry *s*-tetrachloroethane (20 ml.) (2·5 hours' refluxing). The solvent was steam-distilled and the product, b. p. 222—226°/6 mm., gave the colourless cyclic *ketone* (1 g.), m. p. 53—54° [from light petroleum (b. p. <40°)] (Found : C, 86·5; H, 6·2. $C_{18}H_{16}O$ requires C, 87·05; H, 6·5%). It acquired a violet colour on exposure to light. Cyclisation (acid chloride) with aluminium chloride or fuming stannic chloride gave a poor yield.

1′ : 2′ : 3′ : 4′-*Tetrahydro-3′-methyl-2* : 3-*benzofluorene.*—The above ketone (0·6 g.) was reduced with lithium aluminium hydride (0·5 g.) in the usual manner. The product, b. p. 225—235°/8 mm., gave 1′ : 2′ : 3′ : 4′-*tetrahydro-3′-methyl-2* : 3-*benzofluorene* (0·4 g.), colourless needles, m. p. 151—152° (from methanol) (Found : C, 92·8; H, 7·5. $C_{18}H_{18}$ requires C, 92·3; H, 7·7%). Reduction by the modified Clemmensen method was unsuccessful.

3′-*Methyl-2* : 3-*benzofluorene* (XV).—The tetrahydrobenzofluorene (0·5 g.) was heated with sulphur (0·3 g.) at 280—290° for 1 hr. 3′-*Methyl-2* : 3-*benzofluorene* (0·2 g.) was obtained in pale yellow crystals, m. p. 114—115° [from benzene–light petroleum (b. p. 60—80°)] depressed to 80—87° on admixture with the tetrahydro-compound (Found : C, 92·9; H, 5·9. $C_{18}H_{14}$ requires C, 93·9; H, 6·1%).

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Nucleotides. Part XXXI. The Stepwise Degradation of Polyribonucleotides: Model Experiments.*

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The fundamental requirements for a stepwise degradation of polyribonucleotides are delineated and a method is evolved, in model experiments, depending on the easy base-catalysed elimination reaction undergone by esters of β-hydroxy-carbonyl compounds. Oxidation of adenosine-5′ phosphate and adenosine-5′ benzyl phosphate by periodate to the corresponding dialdehydes, followed by very mild treatment with alkali, causes rapid elimination of inorganic phosphate and monobenzyl phosphate respectively. Under the conditions of the reaction no appreciable hydrolysis of the internucleotide linkages in yeast ribonucleic acid occurs.

Recent work in these and other laboratories has led to general structures for the ribonucleic acids. They have been shown to consist of chains of nucleoside residues linked at the 3′- and 5′-positions by phosphodiester groups as in (X) (see, *inter alia* Brown and Todd, *J.*, 1952, 52; 1953, 2040; Brown, Heppel, and Hilmoe, *J.*, 1954, 40; Todd, *Proc. Nat. Acad. Sci. U.S.A.*, 1954, **40**, 748). Two problems are still, however, outstanding. The first relates to the question of chain branching (see, *e.g.*, Brown and Todd, *locc. cit.*), and the second to the sequence of the individual nucleotide residues in ribonucleic acids. A successful solution to the latter problem could only be achieved if the homogeneity of a given ribonucleic acid were proved. If, as seems certain, the ribonucleic acids, like the deoxyribonucleic acids, are mixtures of different molecular species efforts to determine end-groups or nucleotide sequence would be of little value, except possibly as a criterion of homogeneity, during fractionation. Nevertheless a method of stepwise degradation would be of considerable value quite apart from its application to intact ribonucleic acids, since only by its use could the structures of the larger oligonucleotides (see, *e.g.*, Volkin and Cohn, *J. Biol. Chem.*, 1953, **205**, 767) be determined. A method has now been evolved and has been briefly reported (Brown, Fried, and Todd, *Chem. and Ind.*, 1953, 352) which, it was pointed out, could in theory also give information regarding the first problem, namely, the nature and extent of any chain-branching present in a given polynucleotide.

The fundamental problem in the determination of residue sequence in a polynucleotide is the discovery of a method of differentiating the terminal phosphodiester linkage from all other similar linkages in the molecule, so as to allow the removal of the terminal residue, while leaving the rest of the polynucleotide intact and ready for a repetition of the same process. It is clear from present knowledge of the chemistry of the ribonucleic acids, or more generally of alkyl esters of ribonucleotides (Brown and Todd, *locc. cit.*), that the great lability towards alkaline or acid reagents of a phosphodiester system carrying a vicinal hydroxyl function, severely limits the choice of methods. Indeed, it appears, at present, that little, if any, differentiation between the stabilities towards hydrolysis of the various phosphodiester linkages comprising the polynucleotide chain can be made. In any event graded hydrolysis could not be expected to lead solely to removal of terminal residues.

On these grounds, we were led to consider whether an elimination, rather than a hydrolytic process could be used, and how the necessary activating function could be introduced. The ease with which esters of β-hydroxy-carbonyl derivatives undergo base-catalysed elimination reactions is well known. Thus Linstead, Owen, and Webb (*J.*, 1953, 1211) have considered some earlier examples of the reaction and have themselves studied quantitatively the alkali-catalysed elimination of toluene-*p*-sulphonyloxy-, acetoxy-, benzoyloxy-, and, in particular, diphenylphosphonyloxy- and phosphonyloxy-anions from a series of the corresponding β-acyloxy-butyric and -β-phenylpropionic esters (*e.g.*, I → II). Nearer to our theme is the conversion of glyceraldehyde-3 phosphate (III) into lactic acid in very

* Part XXX, *J.*, 1955, 808.

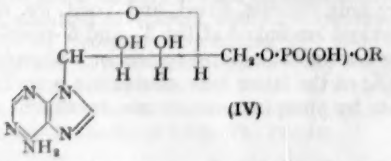
mild alkali and into pyruvaldehyde in presence of acid (Meyerhof and Lohmann, *Biochem. Z.*, 1934, **271**, 89; Baer and Fischer, *J. Biol. Chem.*, 1943, **150**, 223).

$$\underset{\text{(I)}}{>C(OR)\cdot CHR'\cdot CO\cdot R''} + OH^- \longrightarrow \underset{\text{(II)}}{>C{=}CR'\cdot CO\cdot R''} + RO^- + H_2O$$

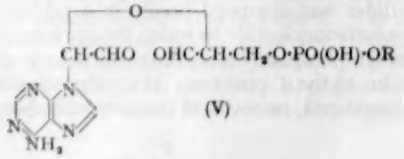
$$OHC\cdot CH(OH)\cdot CH_2\cdot O\cdot PO_3H_2 \xrightarrow[\text{(III)}]{H^+ \text{ or } OH^-} H_3PO_4 + OHC\cdot C(OH){=}CH_2 \xrightarrow{OH^-} HO_2C\cdot CH(OH)\cdot CH_3$$

Zittle (*J. Franklin Inst.*, 1946, **242**, 221) observed that no acid groups are liberated from yeast ribonucleic acid in alkali below pH 10·6. Above that, hydrolysis of the internucleotidic linkages begins. In confirmation, we found that when a solution of yeast ribonucleic acid was brought carefully to pH 10·5, no drop in pH occurred over a considerable period at room temperature, indicating absence of hydrolytic degradation of the polynucleotide. In subsequent experiments on the elimination reaction pH values in the range 10—10·5 were adhered to, as satisfying the main criterion expressed above.

As model substances in the nucleotide series, adenosine-5′ phosphate (IV; R = H) and adenosine-5′ benzyl phosphate (IV; R = CH_2Ph) were chosen, since oxidation to the corresponding dialdehydes (V; R = H and CH_2Ph) can be carried out quantitatively at room temperature in the pH range 5—6. The phosphoryl group in the latter substances is in the β-position with respect to an aldehyde function so that it was expected, by analogy with the examples cited above, that treatment with base would split off phosphate and monobenzyl phosphate respectively. This was found to be the case, when the reaction was studied by paper chromatography, by phosphate estimation, and by titration of liberated acid groups as a function of time.



(IV)



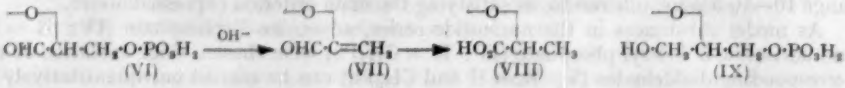
(V)

The dialdehydes were not isolated because of their instability, and so the solutions were studied directly. On paper chromatograms they had a marked tendency to trail. When brought to pH 10·5 with glycine buffer or by careful addition of dilute ammonia solution a rapid reaction appeared to ensue since chromatograms showed that the spot absorbing in the ultraviolet (due to the adenine residue) no longer coincided with that containing phosphorus. In several solvent systems the phosphorus-containing substance from the aldehyde (V; R = H) was identified with inorganic phosphate, and that from the ester (V; R = CH_2Ph) with monobenzyl phosphate. The major ultraviolet-absorbing spot in each case corresponded in R_F value with adenine, and not with the periodate oxidation product from adenosine, which might have been expected had the phosphate residue been removed by hydrolysis rather than elimination. Further work is in progress to elucidate the mechanism of the formation of adenine. In most experiments assessed by chromatography liberation of phosphate or benzyl phosphate appeared complete within a few hours, although, in some, traces of ultraviolet-absorbing material still containing phosphorus remained. Adenosine-5′ phosphate and adenosine-5′ benzyl phosphate were, as expected completely stable at pH 10·5.

In order to obtain a clearer idea of the rate and extent of reaction, the dialdehyde (V; R = H) was brought to pH 10·5 (glycine buffer) and the rate of liberation of inorganic phosphate followed. Reaction appeared to be essentially complete in three hours after 85% of the bound phosphate had been liberated. In another experiment reaction proceeded to the extent of 90%. With the dialdehyde (V; R = CH_2Ph), benzyl phosphate could not be estimated directly. Catalytic debenzylation failed and recourse was had to the specific prostate phosphomonoesterase to hydrolyse the ester to inorganic phosphate which was then estimated. By this means, it was found that at least 71% of benzyl phosphate had been liberated. This figure should be considered as a lower limit in view of the chromatographic

evidence and the possibility of enzyme inhibition. Leaving out any of the above steps, *viz.*, periodate oxidation, treatment at pH 10·5, or enzyme hydrolysis, led to the liberation of negligible amounts of phosphate.

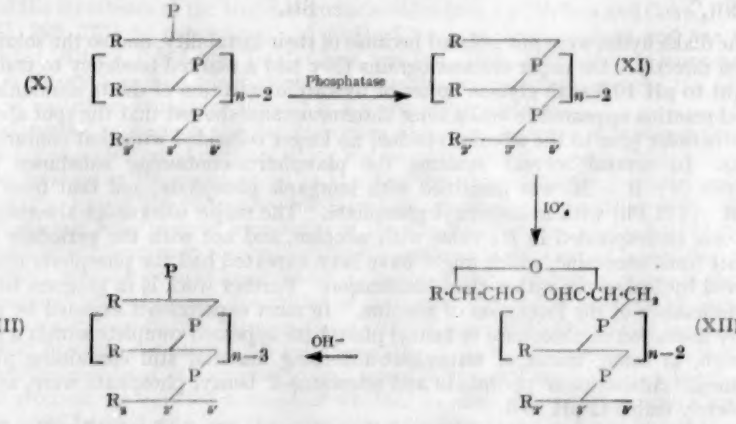
In a further attempt to assess the extent of reaction, solutions of the dialdehydes (V; R = H and CH_2Ph) were brought to pH 10·5 and held at that pH by addition, at intervals, of dilute sodium hydroxide solution. It was observed that over a period of ten hours, 2·04 and 1·9 mols. respectively of alkali were consumed. The reason for the excess of approximately one mol. over that required for the elimination of a phosphate or benzyl phosphate anion is not yet clear. Possible explanations would involve the formation of adenine (pK_a 9·8; Taylor, *J.*, 1948, 765) after the elimination reaction, for which there is already evidence, or an oxidoreduction in the eliminated residue (VI → VIII), or an internal Cannizzarro reaction (cf. Fry, Wilson, and Hudson, *J. Amer. Chem. Soc.*, 1942, **64**, 872). The last reaction would also explain why elimination was incomplete: for if a small amount



(VI) (VII) (VIII) (IX)

of material having the structure shown in the partial formula (IX) were formed by a Cannizzaro reaction, the activation due to the carbonyl function would be lost and elimination would not then proceed. A more detailed study of this aspect of the reaction is being carried out, but it is sufficient at present that the elimination occurs readily at room temperature at a pH of 10·5 to the extent of 85—90%.

The bearing of these model experiments on sequence determination in polyribonucleotides was discussed briefly in a preliminary note (Brown, Fried, and Todd, *loc. cit.*). A polyribonucleotide in which the nucleoside residues are linked at the 3′- and 5′-positions through phosphodiester groups must have either a terminal α-glycol system or a phosphate residue at the 3′-position. If a polynucleotide (X) of the latter type containing *n* residues is considered, removal of the terminal phosphate by phosphomonoesterase treatment will



(In these representations, R represents the heterocyclic nuclei, and the horizontal lines the carbohydrate residues.)

yield (XI) in which only the terminal residue carries an α-glycol system. Oxidation by periodate will then lead to the dialdehyde (XII). That the above reactions can be carried out on polynucleotides has already been shown (Schmidt *et al.*, *J. Biol. Chem.*, 1951, **192**, 715). The dialdehyde (XII) is strictly analogous to the periodate oxidation product (V) from adenosine-5′ benzyl phosphate, the benzyl groups being equivalent to the remainder of the polynucleotide chain. Since we have shown that (V; R = CH_2Ph) readily eliminates

benzyl phosphate, treatment of the analogue (XII) at pH 10·5 should split off the terminal residue, leaving the polynucleotide (XIII) having $(n - 1)$ residues, but otherwise unaltered. The whole process can then be repeated, thus effecting a stepwise degradation. This process is feasible since the degradation has been successfully carried out on several dinucleotides ($n = 2$; Whitfeld and Markham, *Nature*, 1953, **171**, 1151) and trinucleotides ($n = 3$; Whitfeld, *Biochem. J.*, 1954, **58**, 390).

The above method could, in theory, afford evidence as to the presence or absence of chain branching in a ribonucleic acid. The type of branching postulated earlier (Brown and Todd, *J.*, 1952, 52), and for which further evidence has been given (Volkin and Cohn, *J. Biol. Chem.*, 1953, **203**, 319), involved the attachment of side-chains at $C_{(2')}$ of nucleoside residues in the main chain. The presence of such a branch would be revealed if, during a stepwise degradation, phosphomonoesterase removed the terminal phosphate residue giving a molecule which was not oxidisable by periodate, since the side chain at $C_{(2')}$ would preclude the formation of a terminal α-glycol system.

Experimental

Paper-chromatography Studies.—For the paper-chromatographic study of the elimination reaction, solutions were prepared so that a final concentration of *ca.* 10 mg./c.c. was obtained.

Adenosine-5′ phosphate (34·7 mg.) was oxidised with sodium metaperiodate (21·6 mg., 1·1 mol.) in water (1 c.c.) for 24 hr. This solution (0·1 c.c.) was brought to pH 8, 0·25M-glycine buffer (0·2 c.c. of pH 10·5; Internat. Crit. Tables, Vol. I, p. 83) added, and the solution kept at room temperature overnight.

The same procedure was applied to adenosine-5′ benzyl phosphate (Baddiley and Todd, *J.*, 1947, 648).

The solutions were studied on ascending chromatograms (Whatman No. 1 paper), together with standard substances, and some representative results are collected in Table 1. The R_P values of phosphorus-containing (P) and ultraviolet-absorbing (U.V.) spots are recorded. Phosphates were detected by the spray reagent of Hanes and Isherwood (*Nature*, 1949, **164**, 1107). Solvent systems used were: A, *n*-butanol–acetic acid–water (5 : 1 : 4); B, propan-2-ol–water–trichloroacetic acid–ammonia (Abel, *Bull. Soc. chim. France*, 1953, 1089); C, propan-2-ol–water–ammonia (*d* 0·88) (70 : 20 : 10).

Table 1. *R_P values in solvent systems.*

	A		B		C	
Substance	P	U.V.	P	U.V.	P	U.V.
Adenosine-5′ phosphate	0·02	0·02	0·03	0·03	0·06	0·06
Inorg. phosphate	0·072 *	—	0·53 *	—	0·03 *	—
Adenine	—	0·36	—	0·49	—	—
Dialdehyde (V; R = H)	0·13	0·13	0·46	0·46	0·03	0·03
Ditto, treated at pH 10·5	0·07 *	0·37	0·53 *	0·49	0·03 *	—
Adenosine-5′ benzyl phosphate ...	0·42	0·42	0·58	0·58	0·57	0·57
Benzyl dihydrogen phosphate	0·55	—	0·86	—	0·27	—
Adenine	—	0·54	—	0·62	—	0·54
Dialdehyde (V; R = CH_2Ph)	0·60	0·60	0·75	0·75	0·37	0·37
Ditto, treated at pH 10·5	0·55	0·48—0·65	0·86	0·62	0·27	0·54, 0·63

A, B, and C. The dialdehydes gave elongated spots; R_P values refer to the mid-point of the spot. The spots marked with an asterisk developed a yellow colour immediately on spraying, giving added confirmation of the presence of inorganic phosphate.

The R_P values recorded in Table 1 are those of the major spots. In some experiments faint, diffuse streaks were apparent, containing both phosphorus and ultraviolet-absorbing material, suggestive of incomplete reaction. A material with the same R_P value as adenine was the main ultraviolet-absorbing product of the reaction but other products also appeared to be present. Oxidation of adenosine with periodate and treatment at pH 10·5 gave solutions which streaked on chromatograms and evidently contained several substances, but the main spot again corresponded to adenine.

In similar experiments in which very dilute ammonia solution was used to bring the solutions of oxidised adenosine-5′ phosphate to pH *ca.* 11, paper chromatography showed that the reaction was almost complete within 1—10 min.

Eliminations.—Examination by phosphate analysis. (*a*) Adenosine-5′ phosphate. Adenosine-5′ phosphate (anhydrous; 68·1 mg.) was dissolved in 0·025M-sodium metaperiodate

(12·5 c.c.) and set aside for 20 hr. Aliquot parts (2 c.c.) were withdrawn and the excess of periodate was back-titrated with arsenite (cf. Lythgoe and Todd, *J.*, 1944, 592). The uptake of periodate (1·01, 0·97 mol.) showed complete oxidation. To the remaining solution were added 20 c.c. of 0·25M-glycine buffer (pH 10·3), the solution was diluted to 50 c.c., and aliquot parts (2 c.c.) were removed at intervals for estimation of inorganic phosphate and total phosphorus (Allen, *Biochem. J.*, 1946, **34**, 858).

The release of inorganic phosphate as a percentage of total phosphate was: 53 (5 min.); 64 (1 hr.); 85 (3 hr.); 86 (19 hr). In another experiment the results were: 53 (6 hr.); 70 (24 hr.); 82 (48 hr.); 89 (72 hr.). The rate of liberation of phosphate was unaltered when ethylene glycol was added before the buffer, to reduce excess of periodate.

When a solution of periodate-oxidised adenosine-5′ phosphate prepared as above was brought to pH 4·7 by addition of 0·2M-acetate buffer, the amount of phosphate liberated was negligible (only 5·3% in 21 hr.).

In control experiments, the addition of iodate, periodate, or glycine buffer did not affect phosphate analyses.

(*b*) Adenosine-5′ benzyl phosphate. The ester (14·7 mg.) and sodium metaperiodate (14·8 mg., 2·05 mol.) were suspended in water (4 c.c.), and the solution was shaken for 20 hr. to effect oxidation. 0·25M-Glycine buffer (5 c.c.) was added and the solution made up to 10 c.c. Aliquot parts (1 c.c.) were taken at intervals for determination of inorganic phosphate (none found) and total phosphate, and for treatment with prostate phosphatase followed by phosphate determination. The last process was carried out by adding to each aliquot part the enzyme solution [1 c.c.; containing 5 mg. lyophylised prostate extract/10 c.c. (Loring *et al.*, *J. Biol. Chem.*, 1952, **196**, 821)] and 0·2M-acetate buffer (2 c.c.; pH 4·45) (final pH 5·0). The solution was set aside overnight before analysis for inorganic phosphate. Release of phosphate as a percentage of total phosphate was: 20 (5 min.); 37 (1 hr.); 46 (3 hr.); 56 (7 hr.); 60 (23 hr.). In another experiment the results were: 25 (5 min.); 71 (24 hr.).

The enzyme solution (4 c.c.) completely hydrolysed *cyclo*hexylammonium benzyl phosphate (5·0 mg.) in less than 6 hr.

Titration studies. (*a*) Adenosine-5′ phosphate (11·9 mg.) and sodium metaperiodate (11·6 mg., 1·6 mol.) were dissolved in water (5 c.c.) and shaken at room temperature for 21 hr. The solution was brought to pH 10·5 with 0·0108N-sodium hydroxide (Cambridge pH Meter) and then at suitable intervals the amount of sodium hydroxide necessary to maintain that pH was determined. Experiments were carried out with the solution under carbon dioxide-free nitrogen. The titration figures are given in Table 2 together with the calculated values (mol.) for liberation of titratable acidity.

(*b*) Similarly adenosine-5′ benzyl phosphate (9·5 mg.) was oxidised with sodium metaperiodate (10·8 mg., 2·3 mol.) and the experiment carried through as above. The results are given in Table 2.

TABLE 2

Oxidised adenosine-5′ phosphate (0·0343 milliequiv.)				*Oxidised adenosine-5′ benzyl phosphate* (0·0217 milliequiv.)			
Time (hr.)	NaOH (c.c.)	NaOH (milliequiv.)	Acid liberated (mols.)	Time (hr.)	NaOH (c.c.)	NaOH (milliequiv.)	Acid liberated (mols.)
0·25	0·22	0·0024	0·07	0·25	0·39	0·0042	0·19
0·50	0·50	0·0054	0·16	0·50	0·70	0·0076	0·35
0·75	0·75	0·0081	0·24	0·75	0·89	0·0096	0·44
1·0	0·95	0·0103	0·30	1·0	1·04	0·0112	0·52
2·5	1·87	0·0202	0·59	2·0	1·55	0·0167	0·77
4·0	2·92	0·0315	0·92	3·0	2·15	0·0232	1·07
6·0	4·35	0·0469	1·37	5·0	2·95	0·0318	1·47
10·5	6·50	0·0702	2·04	10·0	3·76	0·0406	1·87

In the blank runs on the unoxidised nucleotides, no increase in titratable acidity was found.

(*c*) When a sample of yeast nucleic acid, prepared by dialysis of a commercial product followed by freeze-drying, was dissolved in water and the solution brought to pH 10·5, no further addition of sodium hydroxide was necessary to maintain this pH for the duration of the experiment (3 hours).

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Standard Potentials of Mercury–Mercurous Sulphate Electrodes in Ethylene Glycol–Water Mixtures at 25°.

By C. M. French and Ch. F. Hussain.

[Reprint Order No. 6142.]

The electromotive force of the cell Pt, H_2 (1 atm.)|H_2SO_4(*m*), ethylene glycol (*X*%), H_2O (100−*X*%)|Hg_2SO_4|Hg was measured at 25° for *X* values of 5, 10, 20, and 30. Standard potentials were computed in each case by extrapolation, and the mean ion activity coefficients of sulphuric acid were calculated for the various acid molalities from 0·05 to 1·00 used in this work.

A detailed investigation of the activity coefficient of sulphuric acid in water has been made by Harned and Hamer (*J. Amer. Chem. Soc.*, 1935, **57**, 27). Relatively few data, however, exist for the activity coefficient of sulphuric acid in other solvents. Notable exceptions are the e.m.f. measurements in aqueous acetic acid (McDougal and Blumer, *ibid.*, 1933, **55**, 2236), in methanol–water mixtures (Shibata and Oda, *J. Chem. Soc. Japan*, 1931, **52**, 590), in ethanol–water mixtures (Crockford and Wideman, *J. Phys. Chem.*, 1946, **50**, 418), and in aqueous propan-2-ol (Land and Crockford *J. Amer. Chem. Soc.*, 1950, **72**, 1895). The present investigation was designed to extend this range of solvents and to provide information on the effect of change of solvent, as denoted by its dielectric constant, on the activity coefficient of the solute.

Experimental

Ethylene glycol was purified by the method of Smyth and Walls (*ibid.*, 1931, **53**, 2116) and finally distilled at 4 mm.: it had b. p. 68°/4 mm., d_4^{25} 1·10985, n_D^{25} 1·43057 (lit.; d_4^{25} 1·10987, Gibson and Loeffler, *ibid.*, 1941, **63**, 898; n_D^{25} 1·43055, Smyth and Walls, *loc. cit.*).

Water used for the preparation of solutions was obtained by passing distilled water through a four-foot column packed with " Biodeminrolit " ion-exchange resin.

Mercury was purified by washing it with dilute nitric acid, dilute sodium hydroxide, and water, and subsequent distillation *in vacuo*. Some of this mercury was then used for the electrolytic preparation of mercurous sulphate by Hulett's method (*Phys. Rev.*, 1911, **32**, 257). The mercurous sulphate was then washed by suction with 3M-sulphuric acid and then 8 times with the solution of which the e.m.f. was to be measured; it was then made into a thin paste with the same solution and of such consistency that it flowed readily from a 5-mm. diameter tube. This paste was transferred to the cell so that it covered the mercury electrode to a depth of about 1 cm. In all these operations exposure to bright light was avoided as far as possible, since such exposure causes a darkening of the mercurous sulphate, and the e.m.f. values obtained with its use are somewhat higher and less reliable. The hydrogen electrode consisted of platinum foil 0·4 × 2·5 cm. first cleaned by making it the anode in 6M-hydrochloric acid, then plating it for 3 min. in gold cyanide solution (Clark, *J. Phys. Chem.*, 1928, **32**, 1056). This electrode was then platinized by the method of Popoff, Kuntz, and Snow (*ibid.*, p. 1056). H-Shaped cells were employed, the two limbs being connected *via* a stop-cock. Hydrogen purified by passage over heated copper turnings was passed first through the solution in a saturator and then through the solution to be measured for 2 hr. The latter solution was then drawn into the cell previously filled with hydrogen and left in contact with the electrodes for several hours before readings were commenced.

Electromotive forces were measured by using a Tinsley two-dial thermoelectric-free potentiometer, and a high-sensitivity mirror galvanometer in conjunction with a lamp and scale. Readings were reproducible to within ±0·05 mv. The experimental e.m.f. values were corrected to 1 atm. pressure of dry hydrogen, the measured vapour pressures of the corresponding solutions of sulphuric acid in ethylene glycol–water mixtures being used for this purpose.

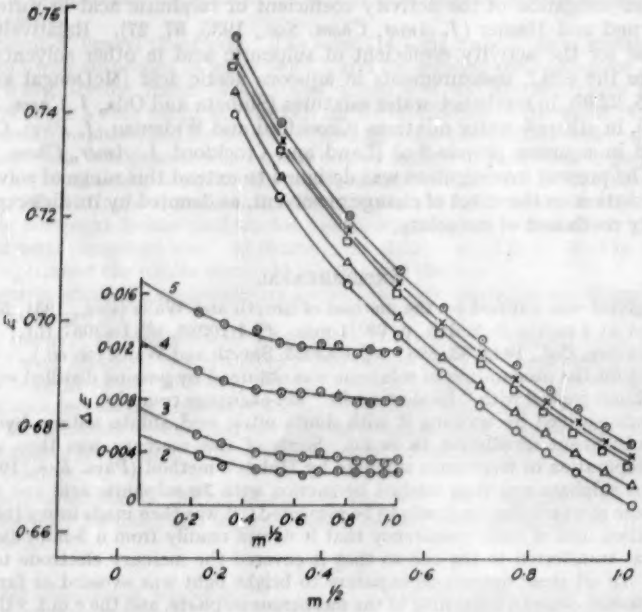
Results and Discussion

In addition to the solutions for which results are given in this paper, measurements were also attempted on solutions of higher glycol content and both greater and smaller

acid concentration. For solutions containing more than 30% of ethylene glycol or of acid concentration greater than 1·0m, the time taken for equilibrium to be established and steady values of e.m.f. to be obtained was so great (>120 hr.) as to render the results somewhat uncertain. Even in the case of 5% ethylene glycol equilibrium was reached only in 40—50 hr. Owing to the solubility of mercurous sulphate, solutions of acid concentration less than 0·05m could not be measured.

Values of the e.m.f. corrected to 1 atm. pressure for solutions of various acid molalities are given in the Table (where d is the density and ε the dielectric constant) together with the mean ion activity coefficients ($\gamma_{\pm}$). These e.m.f. data are compared with similar data for solutions in pure water (Harned and Hamer, *loc. cit.*) in the Figure.

Ethylene glycol concn.: (1, ○) 0, (2, ×) 5%, (3, □) 10%, (4, △) 20%, (5, ○) 30%.



Values of the standard potential for the four solvent media were obtained by the procedure recommended by Land and Crockford (*loc. cit.*), as follows: The values of ΔE, the difference between the measured e.m.f. for the various acid molalities for a given glycol–water mixture and the corresponding values of Harned and Hamer in pure water, were plotted against $m^{\frac{1}{2}}$. The curves thus obtained were nearly linear for concentrations having $m^{\frac{1}{2}}$ greater than 0·4. At lower molalities smooth curves were obtained and extrapolation was accordingly effected to zero molality. The resulting value of ΔE was then subtracted from the value of E° for pure water, the difference representing the value of the standard potential in the aqueous glycol solvent. The latter values are also shown in the Table.

The activity coefficients were calculated from the equation

$$E = E^{\circ} - (3RT/2F) \ln (4^{\frac{1}{3}} m\gamma_{\pm})$$

The activity coefficients γ were calculated on the basis of a reference state of unit activity coefficient of the solute at infinite dilution in the given solvent. The activity coefficients γ' were calculated on the basis of a reference state of unit activity coefficient

for the solute at infinite dilution in pure water. For this purpose the value of E° obtained by Harned and Hamer (*loc. cit.*) was employed.

Molality (m)	d_4^{25}	E.m.f. (E)	$\gamma_\pm$	$\gamma'_\pm$	d_4^{25}	E.m.f. (E)	$\gamma_\pm$	$\gamma'_\pm$
	5% Ethylene glycol (E° 0·6095), ε_{25} = 77·1 D				10% Ethylene glycol (E° 0·6077), ε_{25} = 75·6 D			
0·05	1·0097	0·7505	0·3244	0·3761	1·0161	0·7490	0·3223	0·3911
0·1	1·0127	0·7340	0·2490	0·2882	1·0191	0·7324	0·2480	0·3016
0·2	1·0188	0·7170	0·1935	0·2273	1·0251	0·7158	0·1905	0·2345
0·3	1·0249	0·7068	0·1681	0·1949	1·0310	0·7055	0·1659	0·2016
0·4	1·0309	0·6995	0·1524	0·1766	1·0370	0·6983	0·1500	0·1823
0·5	1·0369	0·6935	0·1421	0·1651	1·0429	0·6922	0·1406	0·1708
0·6	1·0429	0·6884	0·1355	0·1570	1·0488	0·6872	0·1334	0·1620
0·7	1·0488	0·6840	0·1302	0·1510	1·0547	0·6830	0·1275	0·1549
0·8	1·0547	0·6802	0·1257	0·1457	1·0605	0·6793	0·1228	0·1491
0·9	1·0606	0·6766	0·1227	0·1422	1·0664	0·6757	0·1199	0·1456
1·0	1·0666	0·6736	0·1193	0·1384	1·0723	0·6727	0·1166	0·1417
	20% Ethylene glycol (E° 0·6026), ε_{25} = 72·7 D				30% Ethylene glycol (E° 0·5982), ε_{25} = 69·9 D			
0·05	1·0301	0·7441	0·3202	0·4411	1·0434	0·7397	0·3202	0·4978
0·1	1·0330	0·7277	0·2451	0·3398	1·0462	0·7234	0·2444	0·3800
0·2	1·0387	0·7110	0·1892	0·2622	1·0517	0·7067	0·1886	0·2931
0·3	1·0445	0·7007	0·1646	0·2283	1·0573	0·6970	0·1617	0·2507
0·4	1·0503	0·6933	0·1496	0·2075	1·0629	0·6898	0·1462	0·2272
0·5	1·0559	0·6874	0·1395	0·1934	1·0686	0·6840	0·1359	0·2113
0·6	1·0616	0·6827	0·1313	0·1821	1·0744	0·6790	0·1289	0·2004
0·7	1·0673	0·6785	0·1255	0·1741	1·0802	0·6747	0·1236	0·1922
0·8	1·0730	0·6748	0·1209	0·1677	1·0860	0·6709	0·1192	0·1879
0·9	1·0788	0·6712	0·1180	0·1636	1·0917	0·6674	0·1162	0·1806
1·0	1·0846	0·6681	0·1151	0·1596	1·0972	0·6644	0·1131	0·1757

Plots of γ and γ' against the square-root of molality of the acid give curves which show a similar shape to that obtained for pure water. However, the γ values are lower than those for pure aqueous solutions, whereas the values of γ' are higher.

Finally, it may be observed that if E° is plotted against the reciprocal of the dielectric constant for the four solvent media studied, and for water by using the data of Harned and Hamer (*loc. cit.*), a smooth curve is obtained.

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The Synthesis of Compounds with Potential Anti-folic Acid Activity. Part VI. Polyaza-1 : 2-benzanthracene Derivatives.*

By T. S. Osdene and G. M. Timmis.

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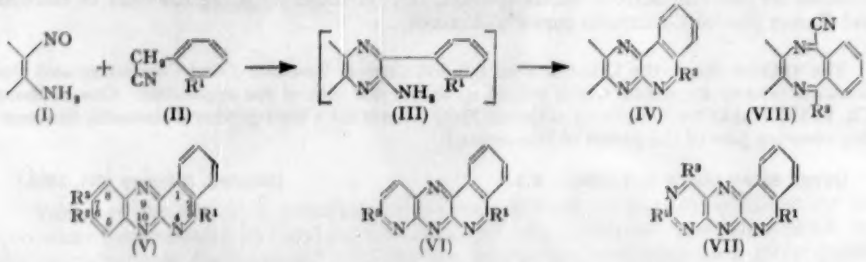
Several derivatives of 4 : 9 : 10-triaza-, 4 : 5 : 9 : 10-tetra-aza-, and 4 : 5 : 7 : 9 : 10-penta-aza-1 : 2-benzanthracene have been prepared unambiguously by condensation of *o*-aminonitroso-derivatives of the benzene, pyridine, and pyrimidine series with suitably *o*-substituted benzyl cyanide derivatives, involving a double ring-closure. The two last-mentioned ring systems are new. Sodium alkoxides in the appropriate alcohol were effective catalysts in most cases.

Although antagonists of folic acid have been usually found amongst analogous pteridines we have investigated considerably more complex ring systems which, however, still embody the pteridine or a closely related structure. Since, for example, Daniel, Norris, Scott, and Heuser (*J. Biol. Chem.*, 1947, **169**, 689) have found high antifolic activity in 6 : 8-diamino-5 : 7 : 9 : 10-tetra-aza-1 : 2 : 3 : 4-dibenzanthracene and Felton, Osdene, and Timmis (*J.*, 1954, 2895) have reported activity in 8 : 8-diamino-5 : 7 : 9 : 10-tetra-aza-1 : 2-benzanthracene, a pentacyclic or tetracyclic structure is not inconsistent with activity. In another field Woolley and Shaw (*J. Biol. Chem.*, 1953, **203**, 979) have found potent antagonists of serotonin, 3-2′-aminoethyl-5-hydroxyindole, amongst simple indole derivatives and an even more potent antagonist in the pentacyclic structure yohimbine; other structures of intermediate complexity containing the indole nucleus are also antagonists. Since we have found that antifolic activity, although of a low degree, is associated with the 6-amino-5-arylpyridino(2′ : 3′-2 : 3)pyrazine (personal communication from Dr. H. O. J. Collier) and 7-amino-6-arylpteridine structures (Spickett and Timmis, *J.*, 1954, 2887) we have now embodied these structures and also that of the corresponding quinoxaline, into more complex types (V, VI, and VII) by completing a six-membered ring between the pyrazine amino-group and the phenyl residue.



Of the ring systems, 4 : 9 : 10-triaza- (V), 4 : 5 : 9 : 10-tetra-aza- (VI) and 4 : 5 : 7 : 9 : 10-penta-aza-1 : 2-benzanthracene (VII), only examples of the first have hitherto been prepared. Gabriel (*Ber.*, 1904, **37**, 4316) and Manuelli and Silvestri (*Gazzetta*, 1904, **34**, I, 493) condensed *o*-phenylenediamine with phthalonimide or phthalonic acid respectively and obtained 3-hydroxy-4 : 9 : 10-tri-aza-1 : 2-benzanthracene (V; $R^1 = OH$, $R^2 = R^3 = H$); Manuelli and Moselli (*ibid.*, 1905, **35**, II, 572) used 1 : 2-diamino-4-methylbenzene to obtain a product (V; $R^1 = OH$, $R^2 = Me$, $R^3 = H$ or *vice versa*). For analogy with the antifolic pyridinopyrazines and pteridines we required a 6-amino-group in our aza-1 : 2-benzanthracenes; by existing synthetic methods, the 1 : 2 : 4-triaminobenzene, 2 : 3 : 6-triaminopyridine, or 2 : 4 : 5-triaminopyrimidine would be condensed with phthalonimide which would in all cases lead to ambiguous structures. Further, by this method only a hydroxy-group can be introduced adjacent to $N_{(4)}$.

* Part V, *J.*, 2036.

We have synthesised unequivocally the required structures by condensing the appropriate *o*-amino-nitroso-compounds with 2-methoxycarbonyl- or 2-carboxy-benzyl cyanide (II; $R^1 = CO_2Me$ or CO_2H) to yield (IV; $R^2 = OH$), or with 2-cyanobenzyl cyanide (II; $R^1 = CN$) to yield (IV; $R^2 = NH_2$). In a preliminary publication (*Chem. and Ind.*, 1954, 404) we briefly reported three of these reactions.

The first stage is assumed to be formation of the intermediate (III) since it has been proved that under similar conditions benzyl cyanides condense with *o*-amino-nitroso-compounds, with loss of water and addition of the amino- to the cyano-group, to form a 2-amino-3-phenylpyrazine (Spickett and Timmis, *J.*, 1954, 2887; Osdene and Timmis, *J.*, 1955, 2032). In order to exclude the unlikely but conceivable alternative structure (VIII) the infrared spectrum of the product (V; $R^1 = OH$, $R^2 = NH_2$, $R^3 = H$) was examined but failed to reveal a band at the frequency 2230 cm.$^{-1}$ characteristic of a cyano-group.

For cyano- or methoxy-benzyl cyanide the reaction is best conducted in boiling ethanol or 2-ethoxyethanol in presence of 1 mol. of the sodium alkoxide. Although 2-carboxybenzyl cyanide does not react appreciably under these conditions, possibly owing to salt formation on the carboxy-group, in boiling acetic acid in presence of sodium acetate this acid with 2 : 4 : 6-triamino-5-nitrosopyrimidine and with 4 : 6-diamino-2-dimethylamino-5-nitrosopyrimidine yields 6 : 8-diamino- (VII; $R^1 = OH$, $R^2 = R^3 = NH_2$) and 8-amino-6-dimethylamino-3-hydroxy-4 : 5 : 7 : 9 : 10-penta-aza-1 : 2-benzanthracene (VII; $R^1 = OH$, $R^2 = NMe_2$, $R^3 = NH_2$) respectively.

For the synthesis of 4 : 9 : 10-triaza-1 : 2-benzanthracene derivatives, 2 : 4-diamino- and 2 : 4-diamino-5-methyl-1-nitrosobenzene were condensed with the ester (II; $R^1 = CO_2Me$) and with the nitrile (II; $R^1 = CN$). The amino-derivatives (V; $R^1 = OH$, $R^2 = NH_2$, $R^3 = Me$) and (V; $R^1 = R^2 = NH_2$, $R^3 = Me$) with boiling acetic anhydride yielded monoacetamido-compounds which were not diazotised by nitrous acid; since both amino-derivatives were diazotised, it is clear that 6-acetamido-derivatives are formed on acetylation.

2 : 6-Diamino-3-nitrosopyridine reacted with the ester (II; $R^1 = CO_2Me$) and nitrile (II; $R^1 = CN$) to give the corresponding 4 : 5 : 9 : 10-tetra-aza-1 : 2-benzanthracene derivatives.

In the preparation of 4 : 5 : 7 : 9 : 10-penta-aza-1 : 2-benzanthracenes, 4 : 6-diamino-, 2 : 4 : 6-triamino-, 4 : 6-diamino-2-dimethylamino-, 4 : 6-diamino-2-methylthio-, and 6-amino-4-hydroxy-2-phenyl-5-nitrosopyrimidines were condensed with the ester (II; $R^2 = CO_2Me$), to yield the corresponding 3-hydroxy-derivatives; and 4 : 6-diamino- and 2 : 4 : 6-triamino-5-nitrosopyrimidine with the cyano-derivative (II; $R^1 = CN$) yielded the corresponding 3-amino-derivatives.

In general, the reaction of 2-cyanobenzyl cyanide with *o*-amino-nitroso-compounds was faster than that of 2-methoxycarbonylbenzyl cyanide. In the latter case at least 1 mol. of sodium alkoxide was desirable since the sodium salt of the product was readily precipitated in good yield. Less than 1 mol. of sodium alkoxide was adequate in the former case, but in all cases the crude product was precipitated during the reaction.

Experimental

M. p.s (uncorrected) were determined in an electrically heated copper block. Analyses were by Mr. P. R. W. Baker, Beckenham. Purity was established by paper chromatography (butanol–acetic acid). The azabenzanthracenes all fluoresce in ultraviolet light. For good yields the conditions prescribed must be adhered to.

2-Methoxycarbonylbenzyl Cyanide.—2-Carboxybenzyl cyanide (*Org. Synth.*, 1942, **22**, 30) (15 g.) in ether (20 ml.) containing 5 drops of acetone was treated gradually with ethereal diazomethane (200 ml.; from 20·6 g. of methylnitrosourea). After 24 hr. at room temperature and drying (KOH), evaporation gave the *ester* (12 g.), needles (from ether or pentane), m. p. 42° (Found: C, 68·5, 68·7; H, 5·5, 5·4; N, 7·9. $C_{10}H_9O_2N$ requires C, 68·6; H, 5·2; N, 8·0%).

2-Cyanobenzyl Cyanide.—2-Cyanobenzyl bromide (Fuson, *J. Amer. Chem. Soc.*, 1926, **48**, 834) (32·0 g.) and " AnalaR " potassium cyanide (13 g.) in ethanol (250 ml.) and water (50 ml.) were gradually brought to the b. p. Vigorous reaction then occurred. After 45 minutes'

refluxing most of the ethanol was removed and the residue was poured into ice–water. The green solid formed was dissolved in chloroform, dried (Na_2SO_4), and passed through alumina. The solvent was removed and the residue crystallised twice from methanol to give white needles, m. p. 79—80° (12·4 g.).

6-Amino-3-hydroxy-4 : 9 : 10-triaza-1 : 2-benzanthracene (V; R^1 = OH; R^2 = NH_2, R^3 = H).—2 : 4-Diamino-1-nitrosobenzene (1·37 g.; finely ground) and 2-methoxycarbonylbenzyl cyanide (1·9 g.) were added to a solution of sodium (0·3 g.) in dry ethanol (100 ml.) and the mixture was boiled under reflux for 30 min. The thick yellow crystalline precipitate was collected after cooling, and crystallised from glacial acetic acid to yield *6-amino-3-hydroxy-4 : 9 : 10-triaza-1 : 2-benzanthracene* as dark orange needles, containing acetic acid of crystallisation, m. p. 336°, which slowly lost acetic acid yielding yellow needles (Found: C, 63·5; H, 4·45; N, 17·3. $C_{15}H_{10}ON_4.CH_3{\cdot}CO_2H$ requires C, 63·4; H, 4·4; N, 17·4. After drying at 120° *in vacuo*: C, 68·7; H, 3·9. $C_{15}H_{10}ON_4$ requires C, 68·7; H, 3·8%). The solution in ethanol showed an intense yellow-green fluorescence in ultraviolet light.

3 : 6-Diamino-4 : 9 : 10-triaza-1 : 2-benzanthracene (V; R^1 = R^2 = NH_2, R^3 = H).—To a solution of sodium (0·1 g.) in dry ethanol (100 ml.) were added 2 : 4-diamino-1-nitrosobenzene (1·37 g.) and 2-cyanobenzyl cyanide (1·56 g.) and the mixture was boiled under reflux for 20 min. A thick yellow, crystalline precipitate was deposited at the b. p. After cooling, the precipitate was dried (2·05 g.) and crystallised from glacial acetic acid to yield 3 : 6-diamino-4 : 9 : 10-triaza-1 : 2-benzanthracene as dark orange crystals, containing two molecules of acetic acid of crystallisation, lost *in vacuo* at 190° to give yellow crystals. The orange compound remained unchanged on treatment with ammonia solution but yielded the yellow compound on treatment with dilute sodium hydroxide solution (Found: C, 58·2; H, 4·9; N, 18·2. $C_{15}H_{11}N_5.2CH_3{\cdot}CO_2H$ requires C, 59·2; H, 4·5; N, 18·4. After drying *in vacuo* at 190°: C, 68·8; H, 4·4. $C_{15}H_{11}N_5$ requires C, 68·95; H, 4·2%).

6-Amino-3-hydroxy-7-methyl-4 : 9 : 10-triaza-1 : 2-benzanthracene (V; R^1 = OH, R^2 = NH_2, R^3 = Me).—2 : 4-Diamino-5-methyl-1-nitrosobenzene (1·5 g.), 2-methoxycarbonylbenzyl cyanide (1·8 g.) and sodium (0·3 g.) in dry ethanol (25 ml.), as in the previous case (reflux for 10 min.; crude yield 1·2 g.), gave, after several crystallisations from acetic acid, the *4 : 9 : 10-triaza-1 : 2-benzanthracene* as orange needles, m. p. 334° (Found, after drying *in vacuo* at 180°: C, 69·2; H, 4·2; N, 20·3. $C_{16}H_{12}ON_4$ requires C, 69·55; H, 4·4; N, 20·3%). Diazotisation and coupling with R salt gave a deep red colour. Treatment with hot acetic anhydride yielded the *6-acetamido-derivative* as yellow needles (from *n*-butanol), m. p. 398° (decomp.) (Found, after drying *in vacuo* at 110°: C, 67·8; H, 4·5; N, 17·5. $C_{18}H_{14}O_2N_4$ requires C, 67·9; H, 4·4; N, 17·6%).

3 : 6-Diamino-7-methyl-4 : 9 : 10-triaza-1 : 2-benzanthracene (V; R^1 = R^2 = NH_2, R^3 = Me).—2 : 4-Diamino-5-methyl-1-nitrosobenzene (1·0 g.), 2-cyanobenzyl cyanide (1·1 g.), and a solution of sodium (0·2 g.) in dry ethanol (20 ml.), as in the previous case, gave, after several crystallisations from dimethylformamide, *3 : 6-diamino-7-methyl-4 : 9 : 10-triaza-1 : 2-benzanthracene* (crude, 1·6 g.), m. p. 363° (Found, after drying *in vacuo* at 180°: C, 69·1; H, 5·3; N, 25·4. $C_{16}H_{13}N_5$ requires C, 69·8; H, 4·8; N, 25·4%). Coupling as before gave a deep red colour.

Hot acetic anhydride yielded the *6-acetamido-derivative* (from *n*-butanol), m. p. 328—329° (decomp.) (dried *in vacuo* at 110°) (Found: C, 69·5; H, 4·6; N, 21·7. $C_{17}H_{15}ON_5$ requires C, 68·1; H, 4·8; N, 22·1%), which failed to diazotise.

6-Amino-3-hydroxy-4 : 5 : 9 : 10-tetra-aza-1 : 2-benzanthracene (VI; R^1 = OH, R^2 = NH_2).—2 : 6-Diamino-3-nitrosopyridine (1·4 g.) and 2-methoxycarbonylbenzyl cyanide (1·4 g.) were added to a solution of sodium (0·3 g.) in ethanol (100 ml.), and the mixture was boiled under reflux for 1 hr. (yellow precipitate). After cooling, the precipitate was collected and extracted with boiling N-acetic acid (30 ml.) to remove some unchanged nitroso-compound. The residue, crystallised several times from dilute formic acid, gave the *tetra-azabenzanthracene* as yellow needles, m. p. >300° (Found: C, 57·9; H, 3·6; N, 22·1. $C_{14}H_9ON_5.H{\cdot}CO_2H$ requires C, 58·25; H, 3·6; N, 22·65. After drying *in vacuo* at 150°: C, 64·0; H, 3·5; N, 26·3. $C_{14}H_9ON_5$ requires C, 63·9; H, 3·45; N, 26·6%). The formic acid solution showed an intense light blue fluorescence in ultraviolet light.

3 : 6-Diamino-4 : 5 : 9 : 10-tetra-aza-1 : 2-benzanthracene (VI; R^1 = R^2 = NH_2).—To a solution of sodium (0·1 g.) in ethanol (100 ml.) was added 2 : 6-diamino-3-nitrosopyridine (1·4 g.), followed by 2-cyanobenzyl cyanide (1·56 g.) and the mixture was boiled under reflux for 1 hr. Several crystallisations from glacial acetic acid yielded the *tetra-azabenzanthracene* as yellow needles (crude, 2·0 g.), m. p. >300° (Found: C, 53·9; H, 5·1; N, 18·9. $C_{14}H_{10}N_6.3CH_3{\cdot}CO_2H$

requires C, 54·3; H, 5·0; N, 19·0. After drying *in vacuo* at 190°: C, 64·3; H, 3·9; loss, 40·8. $C_{14}H_{10}N_6$ requires C, 64·1; H, 3·8; loss, 40·7%).

8-*Amino*-3-*hydroxy*-4 : 5 : 7 : 9 : 10-*penta-aza*-1 : 2-*benzanthracene* (VII; R^1 = OH, R^2 = H, R^3 = NH_2).—**4 : 6-Diamino-5-nitrosopyrimidine** (1·4 g.) and 2-methoxycarbonylbenzyl cyanide (1·8 g.) were added to a solution of sodium (0·25 g.) in ethanol (125 ml.) and the mixture was boiled under reflux for 30 min. (yellow precipitate). After cooling, the precipitate was collected, dried (2·4 g.), recrystallised from 80% formic acid, and basified with 2N-sodium carbonate. Crystallisation of the product from glacial acetic acid yielded **8-*amino*-3-*hydroxy*-4 : 5 : 7 : 9 : 10-*penta-aza*-1 : 2-*benzanthracene*** as light yellow hair-like crystals, m. p. >300° (dried *in vacuo* at 180°) (Found: C, 59·4; H, 2·9; N, 31·6. $C_{13}H_8ON_6$ requires C, 59·1; H, 3·05; N, 31·8%). Hot acetic anhydride yielded the ***8-acetamido-derivative*** as pale yellow needles, m. p. >300° (dried *in vacuo* at 150°) (Found: C, 58·9; H, 3·2; N, 27·75. $C_{15}H_{10}O_2N_6$ requires C, 58·8; H, 3·3; N, 27·4%).

3 : 8-*Diamino*-4 : 5 : 7 : 9 : 10-*penta-aza*-1 : 2-*benzanthracene* (VII; R^1 = R^3 = NH_2, R^2 = H).—**4 : 6-Diamino-5-nitrosopyrimidine** (1·4 g.) and 2-cyanobenzyl cyanide (1·56 g.) were added to a solution of sodium (0·25 g.) in ethanol (125 ml.) and the mixture was boiled under reflux for 10 min. (brown precipitate). After cooling, the material was collected and dried (1·8 g.). Several crystallisations from glacial acetic acid yielded the ***penta-azabenzanthracene*** as yellow crystals (dried *in vacuo* at 190°) (Found: C, 59·65; H, 3·6; N, 36·6. $C_{13}H_9N_7$ requires C, 58·3; H, 3·45; N, 37·25%). The glacial acetic acid solution showed an intense green fluorescence (ultraviolet).

6 : 8-*Diamino*-3-*hydroxy*-4 : 5 : 7 : 9 : 10-*penta-aza*-1 : 2-*benzanthracene* (VII; R^1 = OH, R^2 = R^3 = NH_2).—(*A*) **Finely powdered 2 : 4 : 6-triamino-5-nitrosopyrimidine** (0·75 g.) and 2-methoxycarbonylbenzyl cyanide (1·8 g.) were added to a solution of sodium (0·2 g.) in 2-ethoxyethanol (50 ml.), and the mixture was boiled under reflux for 5·5 hr. (yellow precipitate). Next morning the material was collected and dried (0·5 g.). Several crystallisations from 30% formic acid yielded the ***penta-azabenzanthracene*** as yellow needles, m. p. >300° (dried *in vacuo* at 180°) (Found: C, 54·4; H, 3·3; N, 33·6. $C_{13}H_9ON_7,\frac{1}{2}H_2O$ requires C, 54·2; H, 3·5; N, 34·0%).

(*B*) **2 : 4 : 6-Triamino-5-nitrosopyrimidine** (0·4 g.; finely powdered), 2-carboxybenzyl cyanide (0·45 g.) and anhydrous sodium acetate (0·2 g.) were added to glacial acetic acid (10 ml.), and the whole was boiled under reflux for 30 min. After cooling, filtration, and washing with glacial acetic acid and methanol, the product (0·55 g.) was dissolved in hot 80% formic acid, treated with charcoal, filtered, cooled, and made alkaline with dilute ammonia solution. Recrystallisation of the precipitate from dilute aqueous formic acid yielded very small yellow needles, m. p. >360° (dried *in vacuo* at 180°) (Found: C, 54·8; H, 3·6; N, 33·5. $C_{13}H_9ON_7,\frac{1}{2}H_2O$ requires C, 54·2; H, 3·5; N, 34·0%).

3 : 6 : 8-*Triamino*-4 : 5 : 7 : 9 : 10-*penta-aza*-1 : 2-*benzanthracene* (VII; R^1 = R^2 = R^3 = NH_2).—To a solution of sodium (0·25 g.) in 2-ethoxyethanol (150 ml.) was added **2 : 4 : 6-triamino-5-nitrosopyrimidine** (1·54 g.) followed by 2-cyanobenzyl cyanide (2·0 g.), and the mixture was boiled under reflux for 1 hr. The dense brown precipitate was collected, dried (*in vacuo* at 180° for analysis), analysed (Found: C, 55·1; H, 3·6; N, 39·15. Calc. for $C_{13}H_{10}N_8$: C, 56·1; H, 3·6; N, 40·3%), and crystallised several times from glacial acetic acid, yielding **3 : 6 : 8-*triamino*-4 : 5 : 7 : 9 : 10-*penta-aza*-1 : 2-*benzanthracene*** as yellow needles, m. p. >300° (Found: C, 44·8; H, 5·1; N, 24·8. $C_{13}H_{10}N_8,2CH_3{\cdot}CO_2H,2H_2O$ requires C, 45·1; H, 5·3; N, 24·8%). The acid solution showed an intense green fluorescence (ultraviolet).

8-*Amino*-6-*dimethylamino*-3-*hydroxy*-4 : 5 : 7 : 9 : 10-*penta-aza*-1 : 2-*benzanthracene* (VII; R^1 = OH, R^2 = NMe_2, R^3 = NH_2).—(*A*) **4 : 6-Diamino-2-dimethylamino-5-nitrosopyrimidine** (0·95 g.) and 2-methoxycarbonylbenzyl cyanide (0·9 g.) were added to a solution of sodium (0·25 g.) in ethanol (100 ml.), and the mixture was boiled for 12 hr. The yellow precipitate was collected, dried (0·3 g.), and purified by dissolution in hot 10% formic acid followed by basification with concentrated ammonia solution. The precipitate was recrystallised from butan-2-ol to yield ***8-amino-6-dimethylamino-3-hydroxy*-4 : 5 : 7 : 9 : 10-*penta-aza*-1 : 2-*benzanthracene***, m. p. >300° (dried *in vacuo* at 150°) (Found: C, 58·3; H, 4·35; N, 31·3. $C_{15}H_{13}ON_7$ requires C, 58·6; H, 4·2; N, 31·9%).

(*B*) **4 : 6-Diamino-2-dimethylamino-5-nitrosopyrimidine** (0·5 g.), 2-carboxybenzyl cyanide (0·5 g.), and anhydrous sodium acetate (0·2 g.) were added to glacial acetic acid (10 ml.), and the whole boiled under reflux for 30 min. After cooling and addition of water (20 ml.) the mixture was made alkaline with ammonia solution, the precipitate collected, washed with water and extracted with hot 10% formic acid, the extract treated with charcoal and made alkaline with ammonia solution, and the precipitate collected, washed with methanol, and recrystallised from

butanol, yielding small yellow prisms which did not melt below 360° (dried *in vacuo* at 150°. Found : C, 58·8; H, 4·4; N, 31·5%).

8-*Amino*-3-*hydroxy*-6-*methylthio*-4 : 5 : 7 : 9 : 10-*penta*-*aza*-1 : 2-*benzanthracene* (VII; R^1 = OH, R^2 = MeS, R^3 = NH_2).—4 : 6-Diamino-2-methylthio-5-nitrosopyrimidine (0·9 g.) and 2-methoxycarbonylbenzyl cyanide (0·95 g.) were added to a solution of sodium (0·15 g.) in ethanol (50 ml.), and the mixture was boiled under reflux for 7 min. (yellow precipitate). Several crystallisations from acetic acid afforded the *penta-azabenzanthracene* as yellow needles, m. p. >360° (crude, 1·13 g.) (dried *in vacuo* at 150°) (Found : C, 52·9; H, 3·1; N, 27·0; S, 9·6. $C_{14}H_{10}ON_6S$ requires C, 54·2; H, 3·2; N, 27·1; S, 10·3%). The acetic acid solution showed an intense blue-green fluorescence (ultraviolet).

3 : 8-*Dihydroxy*-6-*phenyl*-4 : 5 : 7 : 9 : 10-*penta*-*aza*-1 : 2-*benzanthracene* (VII; R^1 = R^3 = OH, R^2 = Ph).—A solution of sodium (0·1 g.) in ethanol (50 ml.), 4-amino-6-hydroxy-5-nitroso-2-phenylpyrimidine (0·5 g.), and 2-methoxycarbonylbenzyl cyanide (0·5 g.) as in the preceding case (reflux 1 hr.) gave the *penta-azabenzanthracene* (crude, 0·54 g.) as pale yellow needles, m. p. >300° (Found : C, 63·1; H, 4·0; N, 17·5. $C_{19}H_{11}O_2N_5,CH_3{\cdot}CO_2H$ requires C, 62·8; H, 3·8; N, 17·5. After drying *in vacuo* at 150° : C, 66·4; H, 3·3; N, 20·2. $C_{19}H_{11}O_2N$ requires C, 66·85; H, 3·2; N, 20·5%). The acetic acid solution showed an intense blue fluorescence (ultraviolet).

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Anodic Syntheses. Part XIV. The Use of Acetylenic Components. A New Synthesis of Oleic Acid.*

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The use of (unconjugated) acetylenic acids and half-esters in anodic "crossed" coupling reactions has been examined, and developed into a new synthesis of unsaturated acids.

A study has been made of the partial reduction of acetylenic acids over the Lindlar catalyst.

THE electrolysis of a monocarboxylic acid with a half-ester, and hydrolysis of the initial product, provides a convenient synthesis of fatty acids :

$$R{\cdot}CO_2H + HO_2C{\cdot}[CH_2]_n{\cdot}CO_2Me \longrightarrow R{\cdot}[CH_2]_n{\cdot}CO_2Me \longrightarrow R{\cdot}[CH_2]_n{\cdot}CO_2H$$

The extension of this route to the preparation of the important natural ethylenic acids requires the introduction of an unsaturated grouping, either as such or in some protected form, into one of the two components used in the electrolysis. Obvious groupings are double bonds, their dihydroxy-derivatives, and triple bonds. Provided these were separated from the carboxyl group by at least two carbon atoms, they would not be expected to affect markedly the coupling reaction. The required unsaturated acid would then be obtained directly from an ethylenic component, and from a dihydroxy- or acetylenic component by well-known standard reactions on the initial product.

The examination of some of the above possibilities has been reported in previous papers in this series. Thus *cis*- and *trans*-ethylenic acids and their *erythro*- and *threo*-dihydroxy-derivatives have been shown to couple normally with half-esters, the configuration of the

* Parts IX—XIII, *J.*, 1953, 2393; 1954, 448, 1804, 4219; 1955, 1097.

starting material being fully retained in the product. This provides convenient stereospecific methods for the chain extension of unsaturated fatty acids (Parts IX, X, XII, XIII *).

To complete our initial survey of possible methods for introducing an unsaturated grouping with the monocarboxylic acid component used in the electrolysis, and at the same time to extend our knowledge of the groupings which can be tolerated during coupling reactions of the Kolbe type, we have studied the electrolysis of stearolic (octadec-9-ynoic) acid. Before our work, the behaviour of acetylenic acids at the anode had received very little attention. Only acetylenedicarboxylic acid ($HO_2C{\cdot}C{\equiv}C{\cdot}CO_2H$) and phenylpropiolic acid ($Ph{\cdot}C{\equiv}C{\cdot}CO_2H$) had been examined; as would be expected in view of their αβ-unsaturated structures, neither acid underwent coupling of the Kolbe type (Vanzetti, *Gazzetta*, 1916, **46**, 49).

When electrolysed in methanol with an excess of methyl hydrogen adipate, stearolic acid (I; X = C≡C) behaved normally at the anode, giving tetratriaconta-9 : 25-diyne by symmetrical coupling, and, after hydrolysis, behenolic (docos-13-ynoic; II, X = C≡C) acid in 28% yield by " crossed " coupling with the half-ester. The structure of the acid was confirmed by conversion into erucic acid (see below).

Various anodic chain extensions of the general type,

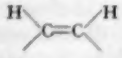
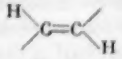
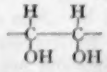
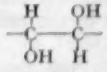
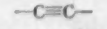
(I) $CH_3{\cdot}[CH_2]_7{\cdot}X{\cdot}[CH_2]_7{\cdot}CO_2H + HO_2C{\cdot}[CH_2]_4{\cdot}CO_2Me$

↓

(II) $CH_3{\cdot}[CH_2]_7{\cdot}X{\cdot}[CH_2]_{11}{\cdot}CO_2H$

where X is an unsaturated group or potential unsaturated centre, are compared in Table 1. The nature of the group X has no great influence on the yield of the product of " crossed " coupling. The choice of starting material for the anodic synthesis of any particular unsaturated acid would therefore be governed primarily by such considerations as its availability, and the ease with which both it and the anodic product can be purified. If a suitable natural acid is readily available, this can be used to prepare a *cis*-acid directly, and will normally be the most convenient starting material [cf. synthesis of erucic (docos-*cis*-13-enoic) and nervonic (tetracos-*cis*-15-enoic) acid from oleic acid (Parts IX and X), and of *cis*-vaccenic (octadec-*cis*-11-enoic) acid from palmitoleic (hexadec-*cis*-9-enoic) acid (Part XII)]. If the natural starting material is difficult to purify, or if it is desired to effect

TABLE 1. *Four-carbon anodic chain extension of unsaturated and hydroxy-acids* (I).

C_{18} Acid	X	Mols. of adipic half-ester	Yield (%) of C_{22} acid *
Oleic [1]		4	34
Elaidic [1]		4	42
erythro-9 : 10-Dihydroxystearic [1]		4·7	34 †
threo-9 : 10-Dihydroxystearic [1]		5·1	27
Stearolic		4	28

* Based on unrecovered C_{18} acid. There was retention of configuration in the first four cases. † Crystalline methyl ester. [1] Bounds, Linstead, and Weedon, *J.*, 1953, 2393.

a stereomutation during the synthesis to give a *trans*-product, then the anodic chain extension of the dihydroxy-derivative may offer advantages [cf. synthesis of *trans*-vaccenic acid from the *threo*-dihydroxy-derivative of palmitoleic acid (Part XII)]. In the absence of a suitable natural starting material a synthetic acetylenic acid may prove most suitable.

Turning to methods for the introduction of an unsaturated centre with a dicarboxylic component, attention has so far been directed to the use of acetylenic intermediates of the

type (VI). By " crossed " coupling first at one end of the molecule with a monocarboxylic acid, and then at the other with a half-ester, a variety of acetylenic acids, and hence, by partial reduction, the corresponding ethylenic acids, could be prepared from a common intermediate. For the method to have a wide scope the value of n must be small. However, previous investigations on the electrolysis of ethylenic monoacids (see summary by Weedon, *Quart. Rev.*, 1952, **6**, 380) suggest that n must be $\not<2$ if normal anodic coupling is to occur. The " limiting " diacid (VI; $n = 2$) was rather inaccessible when these investigations began (Johnson, *J.*, 1946, 1011; see, however, an improved synthesis by Jones, Mansfield, and Whiting, *J.*, 1954, 3208) and we selected the then unknown diacids where $n = 3$ and 4 for initial study in order to confirm the validity of the above proposals. Our work with these intermediates can conveniently be divided into three sections: (i) preparation of the diacids, (ii) their use in anodic " crossed " coupling reactions, and (iii) the partial reduction of the resulting acetylenic acids. We have previously reported the preparation of dodec-6-ynedioic acid (VI; $n = 4$) and its use in the synthesis of tariric (octadec-6-ynoic) and petroselinic (octadec-*cis*-6-enoic) acid (Part XI).

Preparation of Intermediates.—The method described in Part XI for the preparation of the dodecynedioic acid (VI; $n = 4$), and indicated in the reaction scheme below, has been

(III) $Cl\cdot[CH_2]_n\cdot C{\equiv}CH + Br\cdot[CH_2]_n\cdot Cl \longrightarrow Cl\cdot[CH_2]_n\cdot C{\equiv}C\cdot[CH_2]_n\cdot Cl$ (IV) $\longrightarrow$

(V) $NC\cdot[CH_2]_n\cdot C{\equiv}C\cdot[CH_2]_n\cdot CN \longrightarrow HO_2C\cdot[CH_2]_n\cdot C{\equiv}C\cdot[CH_2]_n\cdot CO_2H$ (VI)

examined further. The contaminant of the dichlorodecyne (IV; $n = 4$) is not, as previously suggested, a chlorodecenyne formed by partial dehydrohalogenation, but a chlorododecadiyne (VII) produced in *ca.* 12% yield by self-condensation of the chlorohexyne (III; $n = 4$). The chlorododecadiyne was not isolated, but the crystalline tridecadiynoic acid (VIII) derived from it in the nitrile synthesis was easily separated from the required dodecynedioic acid (VI; $n = 4$). The monoacid was shown by Evans's method (cf. Eglinton and Whiting, *J.*, 1953, 3052) to contain 2 active hydrogen atoms, thus confirming the presence of the ethynyl group ($\cdot C{\equiv}CH$), and on catalytic reduction it absorbed 4 mols. of hydrogen to give tridecanoic acid. When treated under vigorous conditions with alkali it furnished an isomeric acid. By analogy with the rearrangement of other ω-acetylenic acids (Krafft, *Ber.*, 1896, **29**, 2232; Stenhagen, *Arkiv Kemi*, 1949, **1**, 99; Jones, Whitham, and Whiting, *J.*, 1954, 3201), the product is formulated as trideca-6 : 11-diynoic acid (IX).

(VII) $HC{\equiv}C\cdot[CH_2]_4\cdot C{\equiv}C\cdot[CH_2]_4\cdot Cl$ $HC{\equiv}C\cdot[CH_2]_4\cdot C{\equiv}C\cdot[CH_2]_4\cdot CO_2H$ (VIII)

(IX) $CH_3\cdot C{\equiv}C\cdot[CH_2]_3\cdot C{\equiv}C\cdot[CH_2]_4\cdot CO_2H$ $HO_2C\cdot[CH_2]_4\cdot CCl{:}CH\cdot[CH_2]_4\cdot CO_2H$ (X)

Hydrolysis of the dinitrile (V; $n = 4$) with methanolic hydrogen chloride led to the hydrogen chloride adduct (X) of the desired acid.

The second intermediate, dec-5-ynedioic acid (VI; $n = 3$), was prepared from trimethylene bromide chloride by the route developed for its higher homologue. However, the yield on each stage was only about half of that in the series where $n = 4$. This suggests that side reactions may be favoured by some steric factor in the trimethylene series. It is perhaps significant that partial hydrolysis occurred during the preparation of the dinitrile (V; $n = 3$), but none during the preparation of the analogue (V; $n = 4$). In view of the unexpectedly low yields in the preparation of dec-5-ynedioic acid alternative methods are being examined.

Anodic Coupling.—To exemplify the route proposed earlier for the synthesis of acetylenic acids from the intermediates (VI) by two successive anodic coupling reactions, syntheses of stearolic acid were undertaken.

Electrolysis of the half-esters (XI) of dodec-6- and dec-5-ynedioic acid with an excess of pentanoic and hexanoic acid respectively, and hydrolysis of the esters formed by " crossed " coupling, gave pentadec-6-ynoic (XII; $n = 4$) and tetradec-5-ynoic acid (XII; $n = 3$) in 25% yield. A very similar yield (23%) of octadec-6-ynoic (tariric) acid was obtained previously by electrolysis of methyl hydrogen dodec-6-ynedioate with octanoic acid (Part XI). The ability of half-esters of the type (XI) to undergo " crossed " coupling thus seems to be well established.

The conversion of the acetylenic acids (XII) into stearolic acid (XIII) required anodic chain extensions similar to that used in the synthesis of behenolic acid. After pentadec-6-ynoic acid had been electrolysed in methanol with an excess of methyl hydrogen glutarate, considerable difficulty was encountered in purifying the product of " crossed " coupling, and stearolic acid was isolated, *via* the lithium salt, only in low yield (6%). The half-ester

$$CH_3\cdot[CH_2]_{7-n}\cdot CO_2H + HO_2C\cdot[CH_2]_n\cdot C{\equiv}C\cdot[CH_2]_n\cdot CO_2Me \quad (XI)$$

$$\downarrow$$

$$(XII)\quad CH_3\cdot[CH_2]_7\cdot C{\equiv}C\cdot[CH_2]_n\cdot CO_2H + HO_2C\cdot[CH_2]_{7-n}\cdot CO_2Me$$

$$\downarrow$$

$$(XIII)\quad CH_3\cdot[CH_2]_7\cdot C{\equiv}C\cdot[CH_2]_7\cdot CO_2H$$

couples and " cross " couples normally at the anode (cf. Part VIII, Linstead, Lunt, Shephard, and Weedon, *J.*, 1953, 1538; Part X), and we cannot account satisfactorily for the present result. The difficulty may be partly due to some esterification of the pentadecynoic acid with the solvent, accompanying the coupling process and leading to contamination of the product with the starting material. It has recently been shown (Part XIII) that such complications may be avoided by using the benzyl in place of the methyl (or ethyl) hydrogen ester. Chain extension of pentadecynoic acid by means of benzyl hydrogen glutarate might therefore give a better yield of stearolic acid, and will be attempted in due course.

Anodic " crossed " coupling of tetradec-5-ynoic acid with methyl hydrogen adipate took place normally in methanol. After hydrolysis of the initial product, stearolic acid was readily isolated in 24% yield, and identified by direct comparison with an authentic specimen. It yielded stearic acid on complete catalytic hydrogenation.

Partial Reduction of Acetylenic Acids.—The partial reduction of acetylenes has been studied by many previous workers, and widely employed in the synthesis of olefins. Usually chemical methods of reduction give the *trans*-isomer exclusively, whilst catalytic hydrogenation over palladium or nickel gives predominantly the *cis*-isomer (cf. Campbell and Campbell, *Chem. Rev.*, 1942, **31**, 148; Crombie, *Quart. Rev.*, 1952, **6**, 128). In keeping with this generalisation, reduction of stearolic and behenolic acid with zinc and acetic acid is reported to give elaidic (octadec-*trans*-9-enoic) and brassidic (docos-*trans*-13-enoic) acid respectively (Holt, *Ber.*, 1892, **25**, 962; Gonzalez, *Anales Fis. Quim.*, 1926, **24**, 156). Robinson and Robinson (*J.*, 1925, **127**, 175), however, found that treatment of stearolic acid with a mixture of hydrochloric acid, acetic acid, titanous chloride and zinc gave oleic acid; their evidence leaves no doubt that the product had the *cis*-configuration. It is possible that their experiment is related to the recently observed *cis*-reductions of tolane (Ph·C≡C·Ph), [$^2H_2$]acetylene, and [1-^{2}H]propyne with metal-promoted zinc reagents (Rabinovitch and Looney, *J. Amer. Chem. Soc.*, 1953, **75**, 2652). Whether or not the *trans*-acids obtained from stearolic and behenolic acid by the earlier workers using zinc and acetic acid were due to an initial *cis*-addition, followed by an inversion of configuration, is debatable.

Numerous catalytic hydrogenations of acetylenic to the corresponding *cis*-ethylenic fatty acids have been recorded. A W6 Raney nickel catalyst has been used in most of the recent work (Strong *et al.*, *ibid.*, 1948, **70**, 1699, 3391; 1950, **72**, 4263; Huber, *ibid.*, 1951, **73**, 2730; Fusari, Greenlee, and Brown, *J. Amer. Oil Chemists' Soc.*, 1951, **28**, 416; cf. Howton and Davis, *J. Org. Chem.*, 1951, **16**, 1405; Lumb and Smith, *J.*, 1952, 5032). In a careful study of the reduction of stearolic acid by this method, Khan (*J. Amer. Oil Chemists' Soc.*, 1953, **30**, 40) found that fractional crystallisation of the crude product after 1 mol. of hydrogen had been absorbed gave 72% of oleic, 16% of stearolic, and 12% of stearic acid, showing that the catalyst is not completely selective. Infrared examination of the crude product revealed the presence of *ca.* 6% of *trans*-olefin, indicating that the reaction is not completely stereospecific. Other authors have also commented on the formation of small amounts of *trans*-olefins and saturated acids during the half-reduction of acetylenic acids over W6 Raney nickel. These impurities can, however, usually be removed by low-temperature crystallisation.

Relatively little use has been made of palladium catalysts for the partial reduction of

unconjugated acetylenic fatty acids. Paal and Schiedewitz (*Ber.*, 1930, **63**, 766) found that half-hydrogenation of both stearolic and behenolic acid over 1% palladium–barium sulphate gave a mixture of the *cis*- and the *trans*-isomer of the corresponding ethylenic acid, together with the starting material and the saturated acid. We have noted similar lack of stereospecificity and selectivity in the reduction of stearolic acid over 0·5% palladium–calcium carbonate, although this catalyst was reported by Ames and Bowman (*J.*, 1952, 677) to give high yields of the *cis*-olefin from undec-9-ynoic acid. Hofman and Sax (*J. Biol. Chem.*, 1953, **205**, 55) have recommended 5% palladium–charcoal in an alcohol–pyridine medium for the reduction of octadec-11-ynoic acid to the *cis*-olefin; they claim that much less stearic acid is given by this procedure than by the use of W6 Raney nickel.

The conspicuous success of Lindlar's lead–palladium–calcium carbonate catalyst (*Helv. Chim. Acta*, 1952, **35**, 446) in the synthesis of vitamin A and other polyenes from acetylenic intermediates (cf. Weedon, *Ann. Reports*, 1952, **49**, 137) has led us to examine the use of this catalyst for the half-reduction of acetylenic fatty acids. When authentic stearolic acid was reduced over Lindlar catalyst in ethyl acetate, to which a small amount of quinoline had been added for enhanced selectivity (cf. Lindlar, *loc. cit.*), 1 mol. of hydrogen was rapidly absorbed and the reaction then became extremely slow. Crystallisation of the product following Khan's procedure (*loc. cit.*) gave oleic acid in 74% yield, but no stearic or stearolic acid. Reversed-phase chromatography (cf. Howard and Martin, *Biochem. J.*, 1950, **46**, 532), which provides a much more sensitive method for the analysis of mixtures of saturated, ethylenic, and acetylenic acids (Crombie, unpublished results), also failed to detect any significant quantities of stearic or stearolic acid in the "crude" reduction product. An infrared examination of the latter, after esterification with methanol, indicated the presence of about 5% of *trans*-olefin * (cf. Swern, Knight, Shreve, and Heether, *J. Amer. Oil Chemists' Soc.*, 1950, **27**, 17; Ahlers, Brett, and McTaggart, *J. Appl. Chem.*, 1953, **3**, 433). That no migration of the unsaturated centre had occurred during the reduction (cf. Hilditch and Vidyarthi, *Proc. Roy. Soc.*, 1929, *A*, **122**, 552) was shown by comparing the relative quantities of the diacids produced on ozonolysis of stearolic acid, its "crude" reduction product, and purified natural oleic acid. All three samples gave high yields of azelaic acid (see Table 2). The small amounts of other diacids also obtained may be ascribed to secondary reactions during the ozonolysis and the subsequent decomposition of the ozonide (Ackman, Linstead, and Weedon, unpublished results).

TABLE 2. *Ozonolysis of stearolic and oleic acid.*

Acid ozonised	Total yield (%) of diacids	Composition (%) of diacid mixture: azelaic	suberic	pimelic	other acids
Stearolic	86	96·5	*ca.* 1·5	*ca.* 1·5	Trace
Half-reduction product	71	98·5	*ca.* 1	*ca.* 0·5	Trace
Purified natural oleic	79	96	2·5	*ca.* 1	Trace

The results of the various studies on the partial reduction of stearolic acid are summarised in Table 3. For the preparation of oleic acid, the method with the Lindlar catalyst compares favourably with other procedures, and was used to reduce the anodic sample of stearolic acid, thus completing a new total synthesis of oleic acid. Behenolic acid was similarly converted into erucic acid (88%).

Oleic acid has been known since 1813 (cf. Chevreul, "Recherches chimiques sur les corps gras," Imprimerie Nationale, Paris, 1889), and is recognised as the most widespread and abundant fatty acid in Nature. It is therefore not surprising that its synthesis has attracted considerable attention. The first unambiguous synthesis was by Noller and Bannerot (*J. Amer. Chem. Soc.*, 1934, **56**, 1563). This was not a complete synthesis since one of the starting materials was obtained from natural oleic acid. Two total syntheses were reported by Baudart (*Compt. rend.*, 1943, **217**, 399; 1945, **220**, 404; *Bull. Soc. chim. France*, 1946, **13**, 87), and others by Ames and Bowman (*J.*, 1951, 1079) and by Huber (*J. Amer. Chem. Soc.*, 1951, **73**, 2730). However, all these syntheses, with the exception

* [*Added in Proof.*]—This has now been reduced to *ca.* 1—2% by doubling the amount of quinoline used in the reduction.

TABLE 3. *Half-reduction of stearolic acid.*

Authors	Method	Main product: Structure	M. p.	%	By-product
Gonzalez [1]	Zn–AcOH	Elaidic	—	—	—
Robinson and Robinson [2]	Zn–AcOH–$TiCl_3$	Oleic	—	—	—
Adkins and Billica [3]	H_2–W6-Ni	Elaidic [*]	42—45°	—	—
Huber [4]	"	Oleic	10·9—11·5	64	Stearic
Khan [5]	"	"	13·0—13·2	65—71	Stearic + *trans*-olefin + stearolic
Paal and Schiedewitz [6]	H_2–Pd–$BaSO_4$	Oleic + elaidic	—	—	Stearic + stearolic
Present	H_2–Pd–Pb–$CaCO_3$	Oleic	12·8—13·1	74	*trans*-Olefin

[1] *Anales Fis. Quim.*, 1926, **24**, 156. [2] *J.*, 1925, **127**, 175. [3] *J. Amer. Chem. Soc.*, 1948, **70**, 695. [4] *Ibid.*, 1951, **73**, 2730. [5] *J. Amer. Oil Chemists' Soc.*, 1953, **30**, 40. [6] *Ber.*, 1930, **63**, 766.

[*] This claim is at variance with the subsequent experience of other workers, all of whom report high yields of *cis*-olefins when reducing acetylenes over Raney nickel. It is noteworthy that Adkins and Billica cite no evidence, apart from m. p., in support of the structure assigned to their product.

of the last, give mixtures of oleic and elaidic acid in which the latter predominates. Only the present synthesis, and that of Huber which shares the same final stage, gives oleic acid by a route which is substantially stereospecific.

EXPERIMENTAL

M. p.s below 35° were determined after solidification of the molten substance in a capillary tube.

Intermediates.—Acids. Pentanoic acid was prepared by chromic acid oxidation of pure *n*-pentyl alcohol, and hexanoic acid by catalytic hydrogenation of sorbic acid in alcohol over Adams catalyst. The stearolic acid used in the synthesis of behenolic acid, for comparison with the acids synthesised anodically, and in the pilot reduction studies, was obtained by converting (natural) oleic acid into its dibromide and dehydrobromination of the latter with either alcoholic potassium hydroxide (Adkins and Burks, *Org. Synth.*, 1947, **27**, 76) or sodamide in liquid ammonia (Khan, Deatherage, and Brown, *J. Amer. Oil Chemists' Soc.*, 1951, **28**, 27).

Half-esters. Methyl hydrogen glutarate was prepared from glutaric anhydride (Part VIII, *J.*, 1953, 1538). The anhydride was best obtained by a Michael addition of ethyl malonate to methyl acrylate (Marvel and Stoddard, *J. Org. Chem.*, 1938, **3**, 198), and conversion of the resulting triester into glutaric acid (Bachman, Kushner, and Stevenson, *J. Amer. Chem. Soc.*, 1942, **64**, 977), followed by dehydration of the latter with acetic anhydride (Part VIII). Methyl hydrogen adipate was prepared by the method of Swann, Oehler, and Buswell (*Org. Synth.*, Coll. Vol. II, p. 276), and methyl hydrogen dodec-6-ynedioate as described in Part XI.

1-Chloropent-4-yne was prepared from commercial 1-bromo-3-chloropropane (cf. Henne and Greenlee, *J. Amer. Chem. Soc.*, 1945, **67**, 484). The starting material had b. p. 146°, 35—36°/13 mm., n_D^{19} 1·4870, d_4^{25} 1·589, d_4^{20} 1·597. Its bisthiuronium picrate, formed in 55% yield, had m. p. 229—231° (Levy and Campbell, *J.*, 1939, 1442, give m. p. 229°).

Electrolyses.—The cells "A" and "B," and the general procedure followed, were those described in Part IX (*J.*, 1953, 2393). After each electrolysis any solid which had separated was filtered off, the solution was acidified with a slight excess of 2N-hydrochloric acid and then evaporated under reduced pressure. The residue was extracted with ether and the extracts were washed with 0·5N-sodium hydroxide and dried. Acidification of the alkaline washings gave recovered starting materials, if any. The ethereal solution was evaporated and, unless stated otherwise, the residue was then hydrolysed by boiling it with an excess of aqueous-alcoholic potassium hydroxide (10% w/v) for 2—3 hr. in an atmosphere of nitrogen. Dilution with water, and isolation of the acidic fraction in the usual way, gave a product which was extracted with light petroleum (b. p. 40—60°). Crystallisation of the insoluble portion gave the diacid. Evaporation of the petroleum extracts yielded the monoacid.

Ozonolyses.—The unsaturated acids were ozonised at 0° in acetic acid containing 15% of methyl acetate, and the ozonides were decomposed at 35° in acetic acid with hydrogen peroxide (cf. Klenk and Bongard, *Z. physiol. Chem.*, 1952, **290**, 181). The resulting diacids were analysed by paper chromatography (cf. Cheftel, Munier, and Macheboeuf, *Bull. Soc. Chim. biol.*, 1952, **34**, 380; Reid and Lederer, *Biochem. J.*, 1951, **50**, 60).

Behenolic (Docos-13-ynoic) Acid (II; X = C≡C).—Stearolic acid (10·0 g.) and methyl

hydrogen adipate (17·2 g., 3·0 mols.) in methanol (60 c.c.) were electrolysed in cell " B " (current 0·8—1·0 amp.; faradays passed, *ca.* 1·1 times theor.). More half-ester (5·7 g., 1·0 mol.) was added towards the end of the reaction. After the electrolysis, the solid which had separated was collected and crystallised from methanol–light petroleum, giving *tetratriacont-9 : 25-diyne* (0·7 g., 8%) as plates, m. p. 47·5—48° (Found : C, 86·85; H, 13·35. $C_{34}H_{62}$ requires C, 86·7; H, 13·3%).

The methanolic solution from the cell was acidified and evaporated. The residue was extracted with ether, and the extract was washed with alkali and dried. Acidification of the washings gave stearolic acid (0·8 g.), m. p. 45·5—46·5°, and sebacic acid (0·1 g.), m. p. 130—133°. Evaporation of the ethereal solution and distillation of the residue from a Kon flask gave (i) a fraction (10·15 g.), b. p. 90—121°/0·02 mm., which gave sebacic acid (6·0 g.), m. p. 131—133·5°, on hydrolysis, and (ii) a fraction (3·8 g.), b. p. 130—167°/0·02 mm., n_D^{24} 1·4570—1·4575. The latter, together with the high-boiling residue (2·0 g.), was hydrolysed and the acidic fraction was isolated. Crystallisation from aqueous alcohol and then from light petroleum (b. p. 40—60°) gave behenolic acid (3·1 g.), m. p. 57·5—58° (Found : C, 78·6; H, 11·95%; equiv., 341. Calc. for $C_{22}H_{40}O_2$: C, 78·5; H, 12·0%; equiv., 337) (Haussknecht, *Annalen*, 1867, **143**, 40, gives m. p. 57·5°).

A solution of behenolic acid (17·24 mg.) in acetic acid was shaken with Adams catalyst in hydrogen until absorption was complete (2·184 c.c. at N.T.P., equiv., to 1·9 double bonds). Removal of catalyst and solvent gave docosanoic acid (12 mg.), m. p. 79·5—80° (Francis and Piper, *J. Amer. Chem. Soc.*, 1939, **61**, 577, give m. p. 79·95°).

Dodec-6-ynedioic Acid (VI; $n = 4$) *and Trideca-6 : 12-diynoic Acid* (VIII).—Crude dec-5-yno-1 : 10-dinitrile (96 g.), was prepared and hydrolysed as described in Part XI. Crystallisation of the product from benzene gave dodec-6-ynedioic acid (69·5 g.). The benzene mother-liquors were evaporated and the residue was triturated with light petroleum (b. p. 40—60°). Separation and crystallisation of the insoluble fraction from benzene gave more of the diacid (5·3 g.). Evaporation of the petroleum solution, and crystallisation of the residue (11·4 g.), m. p. 35—38°, from light petroleum (b. p. 40—60°) gave *trideca-6 : 12-diynoic acid*, m. p. 39—40° (Found : C, 75·55; H, 8·95%; equiv., 205. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·8%; equiv., 206). This acid, like undec-10-ynoic acid, gave a colourless precipitate with alcoholic silver nitrate; neither undec-10-enoic nor stearolic acid gave this test which requires an ethynyl group. Determination of active hydrogen by Evans's method (cf. Eglinton and Whiting, *J.*, 1953, 3052) gave a value of 1·95 for both the tridecadiynoic acid and undec-10-ynoic acid (indicating 1 acetylenic hydrogen and 1 carboxyl group), and 1·0 for stearolic acid.

Tridecanoic Acid.—A solution of trideca-6 : 12-diynoic acid (529 mg.) in acetic acid was shaken with Adams catalyst (32 mg.) in hydrogen until absorption was complete (241 c.c. at 18°/762 mm., equiv. to 3·95 double bonds). The solvent and catalyst were removed, and the residue was crystallised from aqueous methanol, giving tridecanoic acid (428 mg.), m. p. 41—42° (Found : C, 72·65; H, 12·1%; equiv., 218. Calc. for $C_{13}H_{26}O_2$: C, 72·85; H, 12·25%; equiv., 214) (De Boer, *Nature*, 1927, **119**, 634, gives m. p. 41·2°). The *p*-bromophenacyl ester, prepared in 68% yield, had m. p. 71·5—72° (Found : C, 61·1; H, 7·8. Calc. for $C_{21}H_{31}O_3Br$: C, 61·3; H, 7·6%) (Moses and Reid, *J. Amer. Chem. Soc.*, 1932, **54**, 2101, give m. p. 75°).

Trideca-6 : 11-diynoic Acid (IX).—A solution of trideca-6 : 12-diynoic acid (500 mg.) in 9N-potassium hydroxide–ethylene glycol (5 c.c.) was heated for 1 hr. at 160° (cf. Jones, Whitham, and Whiting, *J.*, 1954, 3201). Isolation of the acidic product in the usual way and crystallisation from light petroleum (b. p. 40—60°) gave *trideca-6 : 11-diynoic acid* (151 mg., 30%), m. p. 36—36·5° (Found : C, 75·5; H, 9·05. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·8%). The acid gave no precipitate with alcoholic silver nitrate. It exhibited no light absorption with $E^{1\%}_{1\,cm.}$ >15 in the region 210—240 mμ.

6-Chlorododec-6-enedioic Acid (X).—Dec-5-yno-1 : 10-dinitrile (2·0 g.) was added to cold (0°) saturated methanolic hydrogen chloride (35 c.c.). The resulting solution was kept at 20° overnight, then evaporated under reduced pressure. Water was added and the product was isolated with ether, giving a liquid (2·6 g.; n_D^{22} 1·4659). Hydrolysis for 2 hr. with boiling aqueous-alcoholic potassium hydroxide (10% w/v) led to an acid (2·25 g., 81%), m. p. 62—63°. Crystallisation from ether–light petroleum (b. p. 40—60°) and then from aqueous methanol gave *6-chlorododec-6-enedioic acid*, m. p. 64—65° (Found : C, 54·95; H, 7·55; O, 24·4, 24·35%; equiv., 133. $C_{12}H_{19}O_4Cl$ requires C, 54·85; H, 7·3; O, 24·35%; equiv., 131).

A solution of the diacid (9·991 mg.) in acetic acid was shaken with Adams catalyst in hydrogen until absorption was complete (1·590 c.c. at N.T.P., equiv. to 1·9 mols.). Removal of catalyst and solvent, and crystallisation of the residue from aqueous methanol, gave

dodecanedioic acid (5·6 mg., 64%), m. p. 126—127·5°, undepressed on admixture with an authentic specimen (Walker and Lumsden, *J.*, 1901, **79**, 1201, give m. p. 126·5—127°).

1 : 8-*Dichloro-oct-4-yne* (IV; $n = 3$).—A solution of sodamide (from 28·6 g. of sodium; cf. Vaughn, Vogt, and Nieuwland, *J. Amer. Chem. Soc.*, 1934, **56**, 2120) in liquid ammonia (1 l.) was added during 2 hr. to a rapidly stirred solution of 1-chloropent-4-yne (133 g.) (Henne and Greenlee, *ibid.*, 1945, **67**, 484) in liquid ammonia (1 l.). After 20 min., 1-bromo-3-chloropropane (208·5 g.) was added during 2·5 hr., and the mixture was stirred overnight. Ammonium chloride (70 g.) was added, and the ammonia was then evaporated. The residue was extracted thoroughly with ether, and the extract was washed with 2N-hydrochloric acid, then with water and dried ($MgSO_4$). Distillation from a Kon flask and refractionation through a Stedman column (20 × 2 cm.) gave 1 : 8-dichloro-oct-4-yne (43·3 g., 19%), b. p. 111—114°/10 mm., n_D^{20} 1·4853—1·4881. A mixture (83 g.) of the chloropentyne and the bromide chloride was recovered.

Oct-4-yno-1 : 8-*dinitrile* (V; $n = 3$) *and Dec-5-ynedioic Acid* (VI; $n = 3$).—A mixture of 1 : 8-dichloro-oct-4-yne (41 g.), sodium iodide (85 g.), and dry acetone (600 c.c.) was stirred and heated under reflux for 22 hr. The solid was filtered off and the solution was evaporated under reduced pressure. The residue was extracted with ether, and the extract was washed with aqueous sodium thiosulphate and dried ($MgSO_4$). Evaporation of the solvent gave crude 1 : 8-di-iodo-oct-4-yne (73 g.). A mixture of the latter, potassium cyanide (40 g.), acetone (190 c.c.), and water (85 c.c.) was heated under reflux for 47 hr. Most of the acetone was distilled off and the residue was extracted with ether. The extract was washed with 2N-sodium hydroxide, aqueous sodium thiosulphate, and then water, and dried ($MgSO_4$). Distillation yielded *oct-4-yno*-1 : 8-*dinitrile* (20 g., 55%), b. p. 97—125°/0·3 mm., n_D^{21} 1·4739 (Found : N, 17·15. $C_{10}H_{12}N_2$ requires N, 17·5%). Acidification of the combined aqueous washings precipitated a solid (1·9 g.) which was collected and had m. p. 103·5—105·5°, undepressed on admixture with the decynedioic acid described below. Acidification of the ether-insoluble portion of the material obtained on evaporation of the acetone gave a nitrogenous acid " Y " (17·5 g.).

A mixture of the dinitrile (18·6 g.), potassium hydroxide (26 g.), water (225 c.c.), and alcohol (120 c.c.) was stirred vigorously, and boiled under reflux for 95 hr. The mixture was cooled and extracted with ether. The aqueous solution was acidified with 6N-hydrochloric acid. The precipitated acid was separated and dried. A further quantity of the crude product was obtained by continuous ether-extraction of the aqueous layer. Crystallisation from benzene gave *dec-5-ynedioic acid* (9·8 g., 43%), m. p. 109—110° (Found : C, 60·75; H, 7·2%; equiv., 102. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%; equiv., 99). Similar alkaline hydrolysis of " Y " also yielded the diacid (4·4 g.). The total yield of decynedioic acid from dichloro-octyne was 30%.

Methyl Dec-5-ynedioate and Methyl Hydrogen Dec-5-ynedioate (XI; $n = 3$).—A mixture of dec-5-ynedioic acid (4·0 g.), absolute methanol (5·0 c.c.), benzene (10 c.c.), and concentrated sulphuric acid (0·6 c.c.) was heated under reflux for 24 hr., and then cooled. Dilution with water and isolation of the neutral product with ether in the usual way gave the *diester* (3·35 g., 79%), b. p. 113—119°/0·5 mm., n_D^{19} 1·4592—1·4615 (Found : C, 63·95; H, 8·15. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%).

A mixture of the diester (3·3 g.), dec-5-ynedioic acid (5·0 g.), *n*-butyl ether (1·0 c.c.), and concentrated hydrochloric acid (0·5 c.c.) was heated at 160°. After 15 min. the temperature was lowered to 130°, methanol (1·0 c.c.) was added, and heating was continued for 4·5 hr., methanol (0·33 c.c.) again being added after 2·5 hr. (cf. Swann, Oehler, and Buswell, *Org. Synth.*, Coll. Vol. II, p. 276). Distillation of the product gave the diester (4·0 g.) and *methyl hydrogen dec-5-ynedioate* (3·3 g.), b. p. 132—142°/0·1 mm., n_D^{20} 1·4682—1·4703 (Found : C, 61·9; H, 7·75. $C_{11}H_{16}O_4$ requires C, 62·25; H, 7·6%).

Pentadec-6-ynoic Acid (XII; $n = 4$).—A solution of pentanoic acid (12·2 g., 3 mols.) and methyl hydrogen dodec-6-ynedioate (9·6 g., 1 mol.) in methanol (60 c.c.) was electrolysed in cell " B " (current 1·2—1·4 amps.; faradays passed, *ca.* 1·3 times theor.). Isolation of the products by the general procedure outlined above, and crystallisation of the diacid fraction (petroleum-insoluble) from aqueous methanol, gave docosa-6 : 16-diynedioic acid (0·35 g., 5%), m. p. 103—103·5°, undepressed on admixture with the sample described in Part XI. (In another experiment the yield of diacid was 9%.) Crystallisation of the monoacid fraction (petroleum-soluble) from aqueous alcohol at 0° gave *pentadec-6-ynoic acid* (1·65 g.), m. p. 25—25·5° (Found : C, 75·75; H, 11·4. $C_{15}H_{26}O_2$ requires C, 75·55; H, 11·0%. Hydrogen no. 128, equiv. to 1·85 double bonds). Distillation of the material recovered from the mother-liquors gave a fraction (1·2 g.), b. p. 90—110° (bath-temp.)/10^{-5} mm., and more of the pentadecynoic acid (0·75 g.; total yield 2·4 g., 25%), b. p. 125—135° (bath-temp.)/10^{-5} mm., m. p. 18—21°.

Redistillation of the combined low-boiling materials from two experiments gave a C_{13} ester

fraction, b. p. 123—126°/11 mm., n_D^{20} 1·4603 (Found: C, 73·5; H, 10·1. Calc. for $C_{12}H_{20}O_2$: C, 73·4; H, 10·25%). This probably consists of methyl undec-6-ynoate and methyl undec-10-en-6-ynoate. Analogous mixtures have been obtained previously in couplings with azelaic (Part IV, Linstead, Lunt, and Weedon, *J.*, 1951, 1130) and β-methylglutaric half-esters (Ställberg-Stenhagen, *Arkiv Kemi*, 1950, **2**, 95).

Tetradec-5-ynoic Acid (XII; $n = 3$).—Hexanoic acid (10·0 g., 2·95 mols.) and methyl hydrogen dec-5-ynedioate (6·2 g., 1 mol.) in methanol (40 c.c.) were electrolysed in cell "A" (current 1·4—1·5 amp.; faradays passed, *ca.* 1·3 times theor.). Isolation of the products by the general procedure gave: (i) *Octadeca-5*: *13-diynedioic acid* (0·25 g., 6%) which crystallised from aqueous methanol and had m. p. 102—104° (Found: C, 70·85; H, 8·5. $C_{18}H_{26}O_4$ requires C, 70·55; H, 8·55%. Hydrogen no. 81, equiv. to 3·8 double bonds). (ii) *Tetradec-5-ynoic acid* (1·75 g., 27%) which crystallised from aqueous methanol (1 : 3) and had m. p. 33—34° (Found: C, 75·0; H, 10·85. $C_{14}H_{24}O_2$ requires C, 74·95; H, 10·8%). A solution of this acid (11·71 mg.) in acetic acid was shaken with Adams catalyst in hydrogen until absorption was complete (2·226 c.c. at N.T.P., equiv. to 1·9 double bonds). Removal of catalyst and solvent, and crystallisation of the residue from aqueous methanol, gave myristic acid, m. p. and mixed m. p. 53—54·5°.

Stearolic (*Octadec-9-ynoic*) *Acid* (XIII).—(*a*) A solution of pentadec-6-ynoic acid (6·4 g., 1 mol.) and methyl hydrogen glutarate (10·0 g., 2·55 mols.) in methanol (30 c.c.) was electrolysed in cell "A" (current 0·6—0·7 amp.; faradays passed, *ca.* 0·95 times theor.). When the current began to drop, more half-ester (3·35 g., 0·85 mol.) was added. The products were isolated in the usual way, and separated into mono- and di-acid fractions with light petroleum. Crystallisation of the crude diacid (3·6 g.) from water (charcoal) gave suberic acid (2·6 g.), m. p. 138—141°. The monoacid fraction, which was only partly solid, was esterified with methanol. The product was distilled and collected in six fractions, b. p. 85—132°/0·15 mm., which were hydrolysed separately. The acidic products in hot methanol were neutralised with aqueous lithium hydroxide. The solutions were evaporated, and the residues were washed with acetone and then crystallised from water at 0°, giving lithium stearolate as needles, m. p. 190—196° (decomp.). Regeneration of the acid from its salt, isolation with ether, and crystallisation from aqueous alcohol gave stearolic acid (0·44 g., 6%), m. p. and mixed m. p. 45—46°.

(*b*) Tetradec-5-ynoic acid (1·55 g., 1 mol.) and methyl hydrogen adipate (3·3 g., 3 mols.; equiv., 161) in methanol (16 c.c.) were electrolysed in cell "A" (current 1·5—1·6 amps; faradays passed, *ca.* 1·25 times theor.). The products were isolated in the usual way, and separated into mono- and di-acid fractions with light petroleum. Crystallisation of the crude diacid from water gave sebacic acid (0·8 g., 38%), m. p. 131—132·5°. Crystallisation of the crude monoacid from aqueous alcohol gave stearolic acid (467 mg., 24%), m. p. and mixed m. p. 45·5—46·5°, unchanged on further recrystallisation (Found: C, 77·0; H, 11·55. Calc. for $C_{18}H_{32}O_2$: C, 77·1; H, 11·5%). A solution of the stearolic acid (13·78 mg.) in acetic acid was shaken with Adams catalyst in hydrogen until absorption was complete (2·226 c.c. at N.T.P., equiv. to 2·0 double bonds). Removal of catalyst and solvent, and crystallisation of the residue from aqueous alcohol, gave stearic acid (9 mg., 63%), m. p. and mixed m. p. 68·5—69°.

Oleic (*Octadec-cis-9-enoic*) *Acid*.—A mixture of Lindlar catalyst (*Helv. Chim. Acta*, 1952, **35**, 446), quinoline (1·2 g.), and ethyl acetate (10 c.c.) was shaken in hydrogen until absorption was complete. A solution of stearolic acid (3·0 g.) in ethyl acetate (60 c.c.) was added, and the mixture was shaken until the absorption of hydrogen became very slow. The reaction was then interrupted, and the catalyst was filtered off (kieselguhr). The filtrate was washed with 2N-hydrochloric acid, then with water, dried ($MgSO_4$), and evaporated. The residue (3·0 g.) had m. p. 11·8—12·8°. Reversed-phase chromatography on paraffin from aqueous acetone gave only one band; the sample was shown to contain <2·5% of stearolic or stearic acid. Ozonolysis of a portion of the "crude" product gave azelaic acid (see Table 2). A further portion was esterified with methanol, and the product was distilled at 10^{-4} mm. Determination of the intensity of the infrared absorption at 10·35 μ of a sample, in carbon disulphide, of the total distillate indicated the presence of *ca.* 5% of *trans*-olefin.

Crystallisation from acetone at −40° of the product from another preparation, identical with that described above, gave oleic acid (2·25 g.), m. p. and mixed m. p. 12·8—13·1°. Similar reduction of the stearolic acid (301 mg.), synthesised anodically, gave oleic acid (235 mg., 78%), m. p. 11·8—12·8°, raised by one crystallisation from acetone at −50° to m. p. 12·3—13·0°.

Reduction of stearolic acid in ethyl acetate, light petroleum (b. p. 60—80°), or alcohol, with Lindlar catalyst without quinoline, gave products containing stearic acid.

Erucic (*Docos-cis-13-enoic*) *Acid*.—Behenolic acid (2·2 g.) in ethyl acetate (80 c.c.) was

reduced over Lindlar catalyst (2·2 g.), containing quinoline (0·88 g.), in the manner described for stearolic acid. Isolation of the product and crystallisation from aqueous alcohol gave erucic acid (1·95 g., 88%), m. p. 31·9—33·7°. After one further crystallisation from the same solvent it had m. p. 33·0—33·5° and did not depress the m. p. of a specimen of the natural acid. Performic acid oxidation (cf. Swern, Billen, Findley, and Scanlan, *J. Amer. Chem. Soc.*, 1945, **67**, 1786) gave *threo*-13 : 14-dihydroxybehenic acid (91%), m. p. and mixed m. p. 100—101° (Dorée and Pepper, *J.*, 1942, 477, give m. p. 101°).

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The Constitution of Some 3-Methylcyclohex-2-enone Dimers.

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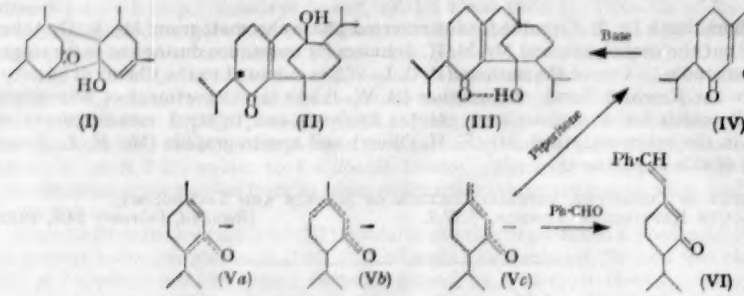
A chemical proof is given for the relationship between the hydroxyl and the αβ-unsaturated carbonyl group in the alkaline dimerisation product of of 3 : 5-dimethyl*cyclo*hex-2-enone. This result uniquely determines the structure of the dimer as well as of α- and β-dipiperitone.

Knoevenagel and Reinecke (*Ber.*, 1899, **32**, 418) first found that 3-methyl*cyclo*hex-2-enones could be dimerised in hot concentrated alkali but they did not propose a structure for the products. Later Ruzicka (*Helv. Chim. Acta*, 1920, **3**, 781) discovered that good yields of the dimers were obtained when powdered sodamide in ether was used in place of aqueous alkali. In the case of 3 : 5-dimethyl*cyclo*hex-2-enone, as a typical example, he proposed the structure (I) for the dimer. Treibs (*Ber.*, 1930, **63**, 2738), in a study of piperitone dimers, suggested a formula for the alkaline dimerisation product, m. p. 105°, but did not present evidence in its support. Briggs, Harland, Ralph, and Simmonds (*J.*, 1953, 3788) in an exhaustive investigation of α- and β-dipiperitone (by-products in the commercial processing of piperitone) showed that Treibs's dimer was a mixture of these two compounds. They also brought considerable evidence forward to support the constitution of the dimer as (II) in which the only difference between the α- and the β-form lay in the stereochemistry of the carbon atom marked with an asterisk. The infrared evidence was claimed to be in good agreement with this assignment. Taylor (*Chem. and Ind.*, 1954, 252), however, has reinterpreted their data to take into account the presence of a strongly hydrogen-bonded αβ-unsaturated carbonyl group (cf. piperitone and the dimers in the Table) and revised the formula to (III) with which all the other evidence agreed. We have remeasured the infrared spectra of some of the dipiperitone derivatives and have found some systematic errors in the results reported by Briggs *et al.* (*loc. cit.*); however, we have not discussed them in this paper since a correction is in the press (Briggs, personal communication).

Cole (*Chem. and Ind.*, 1954, 661) recently pointed out that since these infrared spectra were measured in the solid state this permitted *a priori* the possibility of inter- as well as intra-molecular hydrogen bonding and that spectra should be taken in dilute solution in order to establish the latter type firmly. As can be seen from the Table the spectral results in solution (where taken) were almost identical with those for the solid phase, thus proving intramolecular hydrogen bonding which fully substantiates Taylor's earlier conclusion.

In considering the dimerisation of piperitone it should be noted that of the various

anions (V*a*—*c*) only the simple enol ion (V*a*) and the transoid anion (V*c*) are important. For example the former partakes in the ready racemisation mechanism of optically active piperitones and the latter in condensation reactions under basic conditions, as with benzaldehyde to yield the styryl compound (VI). Hence the Michael addition of piperitone to itself under basic conditions would be expected to give the diketone (IV), subsequent ring closure of which to dipiperitone (III) through an anion of type (V*c*) is clear.



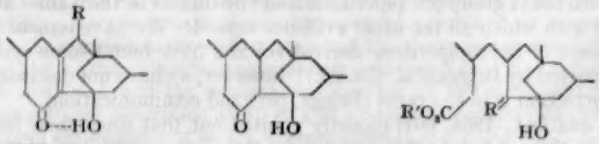
It would be expected then that dimers from other 3-methyl*cyclo*hex-2-enones would have similar structures, and 3 : 5-dimethyl*cyclo*hex-2-enone dimer was chosen for study because it was readily prepared and was crystalline. In agreement with its predicted formula (VII), its infrared and ultraviolet absorption spectra closely resembled those of dipiperitone (see Table). However, it was desirable to obtain more rigid proof and this was done by the following degradation. Reduction of the dimer (VII) in liquid ammonia with a limited

Infrared and ultraviolet maxima of the dimers and their acetates.†

Compound	ν_{OH} (cm.$^{-1}$)	ν_{CO} (cm.$^{-1}$)	$\nu_{C:C}$ (cm.$^{-1}$)	Ultraviolet max. (mμ) (log ε)
α-Dipiperitone (III)	3450	1638	1615	253 (7960), 321 (120)
α-Dipiperitone acetate	—	1735, 1680	1625	247 (8650), 320 (53)
3 : 5-Dimethyl*cyclo*hexenone dimer (VII)	3450, 3472 *	1645, 1650 *	1626, 1625 *	249 (10,200), 315 (100)
Acetate of (VII)	—	1729,* 1673 *	1628 *	246 (10,800)
Piperitone	—	1680	1650	—

* Infrared spectra were taken in KBr mulls unless marked * which were in *ca.* 0·02M-solution in CCl_4.

amount of lithium gave the saturated ketone (X) which despite the proximity of the hydroxy-group had the carbonyl stretching frequency in the normal region. Reduction of the dimer (VII) with excess of lithium in liquid ammonia furnished the saturated diol, and catalytic hydrogenation on the other hand afforded the allylic diol (VII; CH·OH in place of CO) in which the tetrasubstituted double bond was stable to further reduction. The ketone (X) reacted with sodium ethoxide and pentyl nitrite to give in poor yield the hydroxyimino-ester (XI) which on vigorous hydrolysis followed by remethylation with dizaomethane furnished



(VII) R = H
(VIII) R = Br
(IX) R = OEt

(X)

(XI) R' = Et; R = :N·OH
(XII) R' = Me; R = :O

the oily oxo-ester (XII). In agreement with this formulation this ketol-ester (XII) consumed one mol. of lead tetra-acetate; the reaction was slow (24 hours for completion), undoubtedly owing to steric hindrance about the carbonyl group (cf. hydrolysis of its oxime above). This result, which confirms the deductions made from infrared measurements, uniquely

determines the structure of the dimer as (VII) since none of the other possible formulations could have given this last reaction.

Bromination of the dimer (VII) gave, as in the preparation of 6β-bromocholest-4-en-3-one (Djerassi, Rosenkranz, Romo, Kaufmann, and Pataki, *J. Amer. Chem. Soc.*, 1950, **72**, 4534), the bromo-compound (VIII) with which structure the ultraviolet spectrum was in good agreement (Dorfmann, *Chem. Rev.*, 1953, **53**, 84). Analogously to cases observed by Barton and Miller (*J. Amer. Chem. Soc.*, 1950, **72**, 370, 1066, 5309) attempted formation of the 2 : 4-dinitrophenylhydrazone of (VIII) in ethanol gave the corresponding derivative of the ethoxy-compound (IX). Finally we have found that addition of cyanide ion to piperitone gave the expected cyano-ketone and not the dicyclic anhydro-amide postulated by Read and Watters (*J.*, 1929, 2168), and the resistance to hydrolysis of the tertiary cyano-group must be due to steric hinderance.

Experimental

Absorption spectra were taken in 95% EtOH.

1-*Hydroxy*-5 : 9 : 11-*trimethyl*tricyclo[7 : 3 : 1 : $0^{2,7}$]*tridec*-2(7)-*en*-3-*one* (VII).—This was prepared by dimerisation of 3 : 5-dimethyl*cyclo*hex-2-enone and had m. p. 120° from aqueous ethanol [Found : C, 77·3; H, 9·7%; *M* (Rast), 214. Calc. for $C_{16}H_{24}O_2$: C, 77·4; H, 9·7%; *M*, 248]. The 2 : 4-*dinitrophenylhydrazone* had m. p. 191° (from ethanol) (Found : C, 61·6; H, 6·6. $C_{22}H_{28}O_5N_4$ requires C, 61·6; H, 6·6%) and had absorption max. at 260 and 378 mμ (log ε 3·97 and 4·28). The acetate prepared by the acetic anhydride–perchloric acid method was a viscous oil, b. p. 115—120°/0·1 mm. (Found : Ac, 17·8. Calc. for $C_{18}H_{26}O_3$: Ac, 14·8%). The infrared spectrum is unsymmetrical on the high-frequency side, indicating the presence of a little enol acetate and thus accounting for the relatively high acetyl value.

Ketone (X).—The dimer (9·4 g.) in dry ether (500 ml.) was slowly added with stirring to liquid ammonia (400 ml.), and lithium (760 mg.) was added portionwise at the same time at such a rate that the solution remained blue. After completion of the reaction the solution was stirred for 15 min., then *tert.*-butyl alcohol (25 ml.) in ether (25 ml.) was added and ½ hr. later the whole was diluted with more ether, followed by water (200 ml.). The ethereal layer was dried (Na_2SO_4) and yielded on evaporation an oil which, crystallised readily from light petroleum (b. p. 60—80°) and then from ethanol, gave the *ketone*, m. p. 124° (Found : C, 76·7; H, 10·4. $C_{16}H_{26}O_2$ requires C, 76·8; H, 10·5%). The 2 : 4-*dinitrophenylhydrazone*, crystallised from chloroform–ethanol, had m. p. 208° (Found : C, 61·4; H, 7·1; N, 13·1. $C_{22}H_{30}O_5N_4$ requires C, 61·4; H, 7·0; N, 13·0%).

1 : 3-*Dihydroxy*-5 : 9 : 11-*trimethyl*tricyclo[7 : 3 : 1 : $0^{2,7}$]*tridecane*.—Reduction of the above ketone with lithium aluminium hydride in ether afforded the *diol*, a viscous oil which was purified by distillation at 0·5 mm. (bath-temp. 150°) (Found : C, 76·2; H, 11·2. $C_{16}H_{28}O_2$ requires C, 76·1; H, 11·2%).

1 : 3-*Dihydroxy*-5 : 9 : 11-*trimethyl*tricyclo[7 : 3 : 1 : $0^{2,7}$]*tridec*-2(7)-*ene*.—The dimer (2·6 g.) took up only one mol. of hydrogen in acetic acid in the presence of Adams catalyst. The *diol* (2·2 g.), crystallised from ether, had m. p. 111—114°; it did not react with Brady's reagent and showed only strong end-absorption in the ultraviolet region. Oxidation of the diol by chromic acid in pyridine regenerated the dimer in high yield.

Ketol-ester (XII).—Pentyl nitrite (0·4 ml.) was added to an ice-cold solution of the ketone (X) (1 g.) in dry ethanol (15 ml.) in which sodium (100 mg.) was dissolved. After 1 hr. the solution was allowed to warm to room temperature during several hours, then diluted with water, whereupon a precipitate (0·6 g.) of unchanged ketone was recovered. Carbon dioxide was bubbled through the mother-liquor until the pH was 7·5, then the solution was extracted with ether. The resulting aqueous solution was acidified and yielded from its ether extract the oily hydroxyimino-acid (0·2 g.) which was refluxed vigorously for 8 hr., to furnish the ketol-acid (180 mg.). Esterification with diazomethane in ether gave the oily *ketol-ester* (130 mg.), which distilled at 170—175°/1 mm. (Found : C, 68·4; H, 9·2. $C_{17}H_{28}O_4$ requires C, 68·9; H, 9·5%). The ketol-ester had a final uptake of one mol. of lead tetra-acetate in acetic acid in 24 hr.

Bromo-compound (VIII).—Bromine (1·30 g.) in acetic acid (10 ml.) was slowly added to the dimer (1·47 g.) in acetic acid (25 ml.). The mixture was poured into ice-water (200 ml.), and the precipitated 8-*bromo-compound* was filtered off and washed successively with water, sodium hydrogen carbonate, and water then crystallised from ethanol; it had m. p. 114—115° (Found :

C, 58·2; H, 7·3. $C_{14}H_{23}O_3Br$ requires C, 58·7; H, 7·1%). The ultraviolet absorption spectrum showed a max. at 259 mμ (log ε 3·92).

Ethoxy-compound (IX).—The above bromo-compound (100 mg.), 2 : 4-dinitrophenylhydrazine (73 mg.), and concentrated hydrochloric acid (0·3 ml.) were refluxed for 5 min. in ethanol. On cooling, the 2 : 4-*dinitrophenylhydrazone* of the 8-ethoxy-compound crystallised and was pure after four crystallisations from the same solvent, having m. p. 185° (Found : C, 60·7; H, 7·1; N, 12·1; OEt, 8·2. $C_{24}H_{32}O_6N_4$ requires C, 61·0; H, 6·8; N, 11·9; OEt, 9·5%).

5-Cyano-5-methyl-2-isopropylcyclohexanone.—This *ketone* was prepared from piperitone and potassium cyanide according to Read and Watters's method (*loc. cit.*) and had b. p. 151—153°/13 mm. (Found : C, 73·5; H, 9·7; N, 7·4. $C_{11}H_{17}ON$ requires C, 73·7; H, 9·5; N, 7·9%). The infrared spectrum showed bands at 1708 (CO) and 2240 cm.$^{-1}$ (CN). The compound did not form a 2 : 4-dinitrophenylhydrazone.

We are indebted to the National Research Council of Canada for a grant and a N.R.C. Studentship (to W. A. A.), and to Dr. A. R. H. Cole for the determination of some of the infrared spectra.

University of New Brunswick, Fredericton, Canada. [*Received, March 8th*, 1955.]

Some Physical Properties of Nitryl Fluoride.

By G. Hetherington and P. L. Robinson.

[Reprint Order No. 6222.]

This paper adds to the rather few data available on the physical properties of nitryl fluoride, its density, surface tension, and viscosity within the range −120° to −65°. An experimental value for the critical temperature, in agreement with that derived from densities and surface tensions, is given. The properties of nitryl chloride, the only other nitryl halide known, are tabulated for comparison.

The density, freezing point, boiling point, and vapour pressure of liquid nitryl fluoride were determined by Ruff, Menzel, and Neumann (*Z. anorg. Chem.*, 1932, **208**, 293)—previous work was on material of doubtful authenticity—but, as yet, data for the surface tension, viscosity and critical temperature have not been available. Measurements of these, together with a redetermination of the density, are now provided.

The densities of nitryl fluoride in Table 1 are the results of two experiments. They cover a range of temperature from −103·8° to −64·6°, are expressed by the relationship $d_L = 2{\cdot}046 - 0{\cdot}00276T$ g. cm.$^{-3}$, and have a root mean square deviation from the calculated

Table 1.

Expt. 1.

Temp. (° K)	d_L (g. cm.$^{-3}$) Obs.	Calc.	Δd_L	Temp. (° K)	d_L (g. cm.$^{-3}$) Obs.	Calc.	Δd_L
169·2	1·577	1·579	−0·002	200·2	1·493	1·493	0·000
183·7	1·539	1·539	0·000	203·2	1·483	1·485	−0·002
186·2	1·532	1·532	0·000	206·4	1·476	1·476	0·000
194·2	1·511	1·510	+0·001	208·4	1·472	1·471	+0·001
198·7	1·501	1·498	+0·003				

Expt. 2

171·7	1·574	1·572	+0·002	196·9	1·503	1·503	0·000
173·2	1·567	1·568	−0·001	200·9	1·489	1·491	−0·002
194·2	1·508	1·510	−0·002	203·4	1·481	1·484	−0·003

values of ±0·002 g. cm.$^{-3}$. This gives densities which agree well with those derived from the equation of Ruff *et al.* (*idem, loc. cit.*), *viz.*, $d_L = 2{\cdot}143 - 0{\cdot}00323T$ g. cm.$^{-3}$.

The coefficient of cubical expansion of the liquid, calculated from the densities for the temperature range, is 0·00118 cm.^{3} cm.$^{-3}$ deg.$^{-1}$.

Measurements of surface tension at three temperatures by differential capillary rise made in a modified arrangement of Mills and Robinson's closed system (*J.*, 1927, 1823) gave the following results:

Temp. (°c)	−114·3	−104·5	− 94·3
Surface tension (dynes cm.$^{-1}$)	29·5	27·6	25·7

The parachor of nitryl fluoride calculated from the density and surface tension is 94·3; that expected for structure (I) is 99·8 (Sugden, "The Parachor and Valency," Routledge, London, 1930, p. 181).

(I)

The slope of the Katayama plot of $\gamma/(D-d)^{2/3}$ against T, where γ is the surface tension (dynes cm.$^{-1}$), D is the density of the liquid, and d that of the vapour (g. cm.$^{-3}$) at the appropriate temperature, indicates a critical temperature (T_C) of 76·3°.

In spite of several explosions, a direct observation was obtained of the liquid passing through its critical temperature; this lies between 75° and 76°. The result agrees well with the calculated value and, when used, gives a boiling point : critical temperature ratio, $T_B : T_C$, of 0·57.

The viscosity of nitryl fluoride was measured in a modified Ostwald viscometer (cf. Maass and Boomer, *J. Amer. Chem. Soc.*, 1922, **44**, 1709; Steacie and Johnson, *ibid.*, 1925, **47**, 754) which was calibrated with benzene at 25° at which temperature it has about the same surface tension as the liquid under investigation.

Table 2 sets out the physical properties of the two known nitryl halides.

TABLE 2.

	Nitryl fluoride	Nitryl chloride
Melting point	−166°	−145°
Boiling point	−72·5°	−15·9°
Density of liquid at 65° above m. p. (g. cm.$^{-3}$)	1·571	1·500
Surface tension at −104·5° (dynes cm.$^{-1}$)	27·6	—
Viscosity (*a*) at 65° above m. p. (P)	0·00572	—
(*b*) at b. p. (P)	0·00460	0·00616
Critical temperature	76·3°	—
Vapour pressure at 65° above m. p. (mm.)	113·8	16·1

EXPERIMENTAL

All apparatus was of Pyrex glass which, when adequately dried, suffered little attack from nitryl fluoride at the relatively low temperatures used. It was cleaned with chromic acid–nitric acid, followed by copious amounts of water and then alcohol, and dried by repeated change of dry air and heating in a vacuum. Prepared by fluorinating sodium nitrite (Aynsley, Hetherington, and Robinson, *J.*, 1954, 1119), the nitryl fluoride was fractionated several times in a vacuum to rid it especially of volatile impurities and finally put in glass bulbs fitted with "break-seal" joints and stored at a low temperature. It was further fractionated in *vacuo* immediately before use and kept in the measuring apparatus for the shortest possible time.

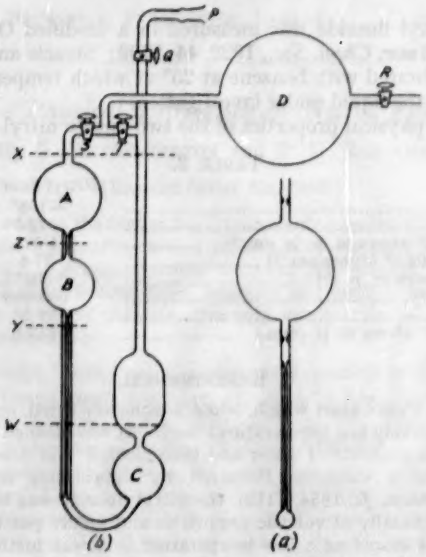
Liquid Density.—The apparatus (*a*, see Fig.) consisted of a small bulb with a calibrated capillary stem. To the stem was joined, by a short length of quill-tubing, a bulb of 200 c.c. capacity which, in turn, was attached to a vacuum train carrying tubes for final fractionation and the break-seal tube of nitryl fluoride. This arrangement enabled the internal surfaces to be thoroughly dried, the liquid to be further fractionated, and an adjusted volume of the purified compound to be transferred to the apparatus and sealed off therein under vacuum. Thus charged, the apparatus was immediately weighed, the capacity of the larger bulb preventing the fluoride from developing a dangerous pressure. Without loss of time, the liquid was completely collected into the small bulb and stem, and frozen there until the larger bulb had been sealed off.

While still cold, the density bulb was supported vertically in a bath of *n*-pentane already cooled to the working temperature with liquid nitrogen in a 1·5 l. clear Dewar vessel, well lagged except for an observation slit, furnished with a magnetic stirrer and a calibrated copper–Constantan thermocouple. The height of the meniscus at a series of temperatures was observed with a cathetometer. Volumes are considered accurate to $\pm 1 \times 10^{-4}$ c.c. and temperatures to ±0·2°. The weighing of the nitryl fluoride was at once completed by freezing the liquid, breaking open the stem, removing the contents, and weighing the pieces along with the large bulb.

Surface Tension.—The apparatus, a slightly modified version of Mills and Robinson's (*loc.*

cit.), held two capillary tubes carefully selected for uniformity of bore. The mean radius of each was ascertained by accurately measuring the length of a mercury thread in overlapping positions. After scrupulous cleaning and rigorous drying on a vacuum train carrying traps and a break-seal vessel of nitryl fluoride, the latter was opened, and some liquid quickly fractionated into a trap and there frozen. In order to minimise the time of contact with the capillary tubes, the liquid was not distilled, but quickly poured into the well-cooled apparatus where it immediately froze. With all speed, the apparatus was detached and mounted in the *n*-pentane bath at near the working temperature. Here the nitryl fluoride melted and, as soon as it reached bath temperature, was caused to flow up the tubes by tilting the apparatus. The difference in the heights of the fallen menisci was measured with a cathetometer and the operations of wetting and measuring were repeated at two other temperatures. An accuracy of $\pm 0{\cdot}2$ dyne cm.$^{-1}$ is claimed.

Critical Temperature.—The procedure and precautions described above being followed, nitryl fluoride was condensed into a heavy-walled (3 mm.) Pyrex tube, 5 cm. long and with specially thickened draw-offs (cf. Parker and Robinson, *J.*, 1927, 2977). When about one-



third full, the liquid was frozen and the tube was drawn off to leave a heavy seal. The critical-temperature tube was kept in a well-stirred water-bath which was slowly heated until the meniscus disappeared, and then cooled until it reappeared again. There was some decomposition and some attack on the tubes, several of which exploded at, or near, the critical temperature. An accuracy of $\pm 0{\cdot}5°$ is claimed.

Viscosity.—The modified Ostwald viscometer (*b*, see Fig.) had a bulb *C* of about the same size as the measuring bulb *B*, to simplify the process of charging with the correct volume of nitryl fluoride. The taps, lubricated with a fluorocarbon grease immune to the fluoride, and the 100 c.c. bulb *D*, enabled the apparatus to be filled and the liquid manipulated. The procedure was to attach, by the socket *P*, the clean dry viscometer to the train delivering nitryl fluoride and, after further drying with *S* and *T* open, to condense liquid in a vacuum until it reached *W*. After *Q* had been closed, the apparatus was detached from the train, the liquid was frozen, and dry air admitted, *via R*, to a pressure of one atmosphere. The viscometer was submerged to level *X* in the *n*-pentane bath; and, as soon as it melted, the fluoride was rapidly raised above level *Z* by an appropriate heating and cooling of *D* and turning of taps *S* and *T*. Then *S* and *T* were opened to equalise the pressure, and the fall of the liquid between *Z* and *Y* was timed. The measurement was repeated at several temperatures, after which the nitryl fluoride was distilled, and finally swept by a current of nitrogen out of *P* to be absorbed, either

in saturated potassium hydroxide solution (Expt. 1) or concentrated sulphuric acid (Expt. 2). In this way its weight was ascertained.

The viscometer had been previously calibrated with benzene at 25°, whence the time of fall of any particular weight, or volume, could be found. The volume of the nitryl fluoride was

TABLE 3.

Expt. 1.

Temp.	η(mP) Obs.	Calc.	Δη	100 $(\Delta\eta)^2$	Temp.	η(mP) Obs.	Calc.	Δη	100$(\Delta\eta)^2$
−113·6°	6·79	6·64	+0·15	2·2	−98·2°	5·55	5·57	−0·02	0·0
−112·0	6·58	6·50	+0·08	0·6	−94·5	5·39	5·38	+0·01	0·0
−111·5	6·53	6·46	+0·07	0·5	−90·8	5·21	5·21	0·00	0·0
−104·5	5·91	5·94	−0·03	0·1	−87·5	5·01	5·08	−0·07	0·5
−102·4	5·75	5·81	−0·06	0·4					

Expt. 2.

−118·5	7·07	7·12	−0·05	0·2	−96·2	5·47	5·46	+0·01	0·0
−116·0	6·87	6·86	+0·01	0·0	−94·0	5·42	5·35	+0·07	0·5
−113·2	6·59	6·60	−0·01	0·0	−88·3	5·16	5·11	+0·05	0·2
−107·0	6·21	6·11	+0·10	1·0	−84·2	5·02	4·95	+0·07	0·5
−102·5	5·89	5·81	+0·08	0·6					

deduced from the density at the temperature of operation. The viscosity was calculated from the expression $\eta = \eta' dt/(d't')$, where η, d, and t are absolute viscosity, density, and time of fall, respectively, of nitryl fluoride, and η', d', and t', the corresponding quantities for benzene at 25°. No attempt was made to correct for the vapour of nitryl fluoride because, at the temperatures used and under one atmosphere pressure of air, the amount is believed to be negligible. The results in Table 3 show a root mean square deviation from the calculated values of ±0·06 mP.

By solving the equation of the absolute viscosity–temperature curve, $\eta_\theta = \eta_0/(1 + A\theta + B\theta^2)$ using values from the smoothed curve, it was found that $A = -0{\cdot}000759$, $B = -0{\cdot}0000384$ and $\eta_0 = 0{\cdot}00392$. This gave an absolute viscosity at the boiling point of nitryl fluoride (−72·5°) of 0·00460 P.

The authors express their indebtedness to the General Chemicals Division of Imperial Chemical Industries Limited, Widnes, for the fluorine cell used, and to the Salters' Company for a Fellowship which enabled one of them (G. H.) to take part in the work.

KING'S COLLEGE, NEWCASTLE-ON-TYNE, 1. [*Received, March 11th*, 1955.]

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*Hydroxybenzotropones. Part I. Synthesis of a Dimethoxybenzo*cyclo*hepta*-1 : 4-*diene*-3 : 7-*dione.*

By A. J. S. SORRIE and R. H. THOMSON.

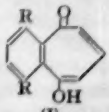
[Reprint Order No. 6171.]

Bromination of the dienol acetate of the dione (II; R = OMe) and subsequent treatment with alkali gave the dione (XV), and not (I; R = OMe). Suppression of enolisation by *peri*-methoxyl groups has a parallel in 4 : 7-dimethoxyindane-1 : 3-dione (XVII).

THE hydroxybenzotropone (I; R = H) was derived by Buchanan (*J.*, 1954, 1060) from the dione (II; R = H). As the dimethoxy-derivative (II; R = OMe) is readily accessible *via* the condensation of quinol and glutaric acid (Bruce, Sorrie, and Thomson, *J.*, 1953, 2403) it was of interest to convert it into (I; R = OMe) and compare the properties of the two hydroxybenzotropones. Some attempts to dehydrogenate the ether (II; R = OMe) by conventional methods are described first; the lack of success was accounted for later when the structure of the final product was elucidated.

Direct dehydrogenation with palladised charcoal in boiling trichlorobenzene, which was effective in the synthesis of αβ-benzotropolone (Cook and Somerville, *Nature*, 1949, **163**, 410; Cook, Gibb, Raphael, and Somerville, *J.*, 1952, 603) and purpurogallin (Caunt,

Crow, Haworth, and Vodez, *J.*, 1950, 1631), resulted only in partial demethylation of our ether (II; R = OMe). Variation of catalyst and solvent, including the incorporation of *p*-nitrotoluene (Blood and Linstead, *J.*, 1952, 2255), the use of chloranil, nitrobenzene–iodine, etc., had no effect on the diketone; sulphur dehydrogenation gave a black tar.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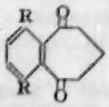
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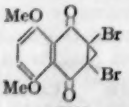
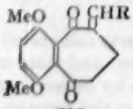

(III)

Dehydrogenation with bromine was readily effected but the brominated compounds obtained (*e.g.*, III) were not soluble in alkali. The structure of these isomeric compounds is considered in the following paper.

In another approach to the conversion of the ether (II; R = OMe) into a hydroxy-tropone we prepared the methylene derivatives (IV; R = Me and Ph) by condensation with acetaldehyde and benzaldehyde respectively, with the object of rearranging these unsaturated ketones to give the hydroxytropones (V; R = Me and Ph). After several failures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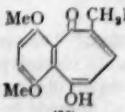
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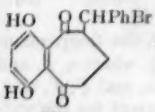
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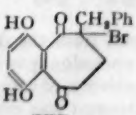
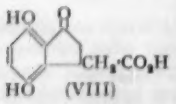

(VII)

with both basic and acidic catalysts, and also palladium–charcoal in high-boiling solvents, this method was abandoned. Leonard and Robinson later (*J. Amer. Chem. Soc.*, 1953, **75**, 2143) successfully rearranged 3 : 7-dibenzylidene*cyclo*heptane-1 : 2-dione to 3 : 7-dibenzyltropolone and found that hydrogen bromide was a specific catalyst and the conditions were critical. We therefore returned to our benzylidene derivative and attempted rearrangement under Leonard and Robinson's conditions. This time starting material was not recovered and two isomeric bromo-compounds were isolated from the benzylidene ether. These arose by addition of hydrogen bromide to the double bond with concurrent demethylation. Remethylation with methyl sulphate and potassium carbonate in acetone also eliminated hydrogen bromide, to give the benzylidene ether (IV; R = Ph); dehydrobromination with pyridine gave the phenol (IV; OH in place of OMe). Both isomers have the same m. p. (the m. p. of a mixture is much lower) but we cannot say whether they are the compounds (VI) and (VII), or two racemic forms of (VI). We were unable to obtain a hydroxytropone from either of these substances.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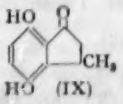
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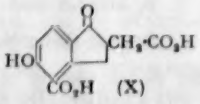
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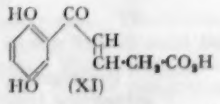

(XI)

In view of the difficulty encountered in dehydrogenating our ether (II; R = OMe) the possibility of avoiding this step was considered. This *might* be achieved in small yield in the first stage of the synthesis by condensing quinol, not with glutaric acid, but with α-chloroglutaric or glutaconic acid, directly to the hydroxytropone (I; R = OH). A trial with glutaconic acid gave the indanone (VIII), which was not surprising. This ketone formed a diacetate and a *p*-nitrophenylhydrazone, and was very similar to 4 : 7-dihydroxy-3-methylindan-1-one (IX). The ultraviolet absorption curves of the two indanones are shown in Fig. 1. A curious feature of the acid (VIII) is its remarkable resistance to decarboxylation. The oxoindanylacetic acid (X) is similar; the benzenoid carboxyl group is readily eliminated but that in the side-chain is not affected by copper chromite in quinoline (Pasternack, Conover, *et al.*, *J. Amer. Chem. Soc.*, 1952, **74**, 1928). The formation of the acid (VIII) clearly proceeds *via* the intermediate (XI) and the reaction is thus analogous to the cyclisation of β-aroylacrylic acids (Baddeley, Holt, and Makar, *J.*, 1952,

3289; Baddeley, Holt, Makar, and Ivinson, *ibid.*, p. 3605) and the formation of indanones by the condensation of naphthalene with maleic anhydride (Lambert and Martin, *Bull. Soc. chim. belges*, 1952, **61**, 132) and of quinol with γ-butyrolactone (Bruce, Sorrie, and Thomson, *loc. cit.*).

Finally we made use of Buchanan's method (*loc. cit.*) to obtain the hydroxybenzotropone (I; R = OMe). (We are indebted to Dr. Buchanan for information prior to publication.) Reaction of the ether (II; R = OMe) with *iso*propenyl acetate gave a mono- (XII) and a di-enol acetate (XIII). Both of these were converted by bromination with *N*-bromosuccinimide and treatment of the oily product with warm methanolic potassium hydroxide into the same compound, regarded initially as the hydroxytropolone (I; R = OMe). When the bromination product (from both mono- and di-enol acetates) was dissolved in pyridine

FIG. 1.

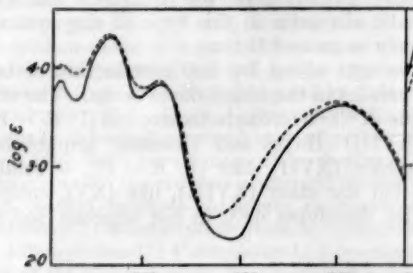
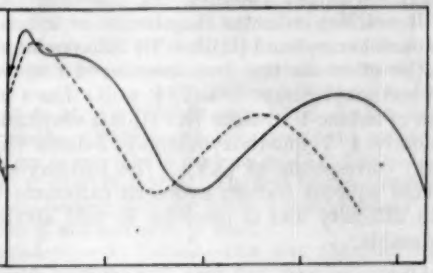


FIG. 2.

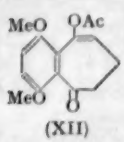


Wave-length (mμ)

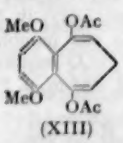
—— 4 : 7-Dihydroxy-3-methylindan-1-one.
– – – 4 : 7-Dihydroxy-3-oxo-1-indanylacetic acid.
Solvent : ethanol.

—— 1′ : 4′-Dimethoxy-1 : 2-benzo*cyclo*hepta-1 : 4-diene-3 : 7-dione.
– – – 1′ : 4′-Dimethoxy-1 : 2-benzo*cyclo*heptene-3 : 7-dione.
Solvent : ethanol.

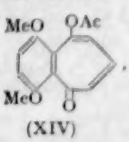
and subsequently poured into dilute hydrobromic acid a pale yellow bromo-derivative, m. p. 125°, $C_{15}H_{15}O_5Br$, was isolated. It became black on storage. Further treatment of this with aqueous or alcoholic alkali gave the same final product in very low yield.



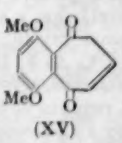
(XII)



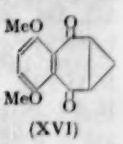
(XIII)



(XIV)



(XV)

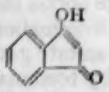
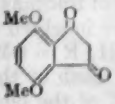


(XVI)

From this it seems that the intermediate bromo-compound is either (XIV), which is improbable, or the bromoacetate of (I; R = OMe). If the acetate groups are partially brominated by reaction with *N*-bromosuccinimide it would account for the low overall yield in the synthesis of the benzotropones (I; R = H and OMe).

The final product was a yellow, crystalline solid, m. p. 163—164°, forming a pale yellow solution in hot aqueous sodium carbonate and warm aqueous sodium hydroxide. It dissolved in concentrated hydrochloric acid, as does the ether (II; R = OMe), and gave no ferric colour or picrate. Attempts to isolate a hydrochloride led to decomposition. No hydroxyl derivatives could be obtained under standard conditions and no pure monocarbonyl derivatives could be isolated, but a dioxime was readily obtained. The compound is thus very different from the hydroxybenzotropone (I; R = H) and is formulated as (XV). This is supported by the results of catalytic hydrogenation [uptake of one mol. of hydrogen regenerated the original dione (II; R = OMe)], the ultraviolet spectrum [compared with that of (II; R = OMe) in (Fig. 2)], and the infrared spectrum which shows a broad carbonyl band at 1678 cm.$^{-1}$ (it could not be resolved) and no hydroxyl band in

the 3-μ region. Most of these results also support structure (XVI) equally, but it is difficult to see how (XVI) could arise from (XIII) and since the compound dissolves in, and can be recovered from, alkali, structure (XVI) seems to be excluded. Infrared bands at 1047 and 990 cm.$^{-1}$ cannot be ascribed to a *cyclo*propane ring (as in XVI), since the ether

(XVII)   (XVIII)

(II; R = OMe) absorbs in the same region having a weak band at 990 and stronger bands at 1016, 1045, and 1060 cm.$^{-1}$. Treatment with hydrobromic acid in acetic acid does not yield a naphthazarin derivative which would be expected from (XVI) (see the following paper). The formation of the diketone (XV) rather than the tropolone analogue (I; R = OMe) indicates the absence of aromatic character in this type of ring system; the parent compound (I; R = H) behaves largely as an enol ketone.

The effect on the seven-membered ring brought about by the introduction of two *peri*-methoxyl groups into (I; R = H) has a parallel in the indanedione series. The enol form of indane-1 : 3-dione (XVII) is a vinylogue of the hydroxybenzotropone (I; R = H). Similarly 4 : 7-dimethoxyindane-1 : 3-dione (XVIII) (Hayes and Thomson, unpublished work) corresponds to (XV). The hydroxy-ketone (XVII), like (I; R = H), is soluble in cold aqueous sodium hydrogen carbonate but the ether (XVIII), like (XV), enolises with difficulty and is insoluble in cold alkalis, dissolving only in hot aqueous sodium hydroxide.

Experimental

4 : 7-*Dihydroxy*-3-*oxo*-1-*indanylacetic Acid* (VIII).—A finely powdered mixture of glutaconic acid (6·4 g.) and quinol (6 g.) was added with stirring to a molten mixture of anhydrous aluminium chloride (90 g.) and sodium chloride (20 g.), at 180—195°. After the addition the mixture was stirred for a further 10 min., cooled, and decomposed with 12% hydrochloric acid (750 ml.). After filtration both precipitate and filtrate were extracted with ether and the combined extracts shaken with aqueous sodium hydrogen carbonate solution. This was acidified and extracted with ether to give, after evaporation, an oil which was washed with a little ethyl acetate, crystallised from ethyl acetate–light petroleum (b. p. 80—90°), and sublimed *in vacuo* as pale yellow crystals, m. p. 208° (0·5 g., 4%) (Found: C, 59·3; H, 4·8. $C_{11}H_{10}O_5$ requires C, 59·45; H, 4·5%). This *acid* gives a green ferric chloride colour. Light absorption: Max. at 206, 232, 256, and 348 mμ (log ε 4·05, 4·32, 3·83, and 3·64 respectively) in MeOH. The orange *p-nitrophenylhydrazone* crystallised from aqueous alcohol as the monohydrate, m. p. 224° (decomp.) (Found: C, 54·3; H, 4·45; H, 10·7. $C_{17}H_{15}O_6N_3.H_2O$ requires C, 54·4; H, 4·55; N, 11·2%). The *diacetate*, crystallised from aqueous methanol, had m. p. 181° (Found: C, 59·1; H, 4·9. $C_{15}H_{14}O_7$ requires C, 58·8; H, 4·6%).

1′ : 4′-*Dihydroxy*-1 : 2-*benzo*cyclo*heptene*-3 : 7-*dione* (II; R = OH).—The procedure of Bruce, Sorrie, and Thomson (*loc. cit.*) was modified to give an increased yield. A mixture of glutaric acid (13·2 g.) and quinol (11 g.) was added slowly with stirring to a molten mixture of anhydrous aluminium chloride (150 g.) and sodium chloride (50 g.); the temperature was maintained at 180—200° throughout the addition (20—30 min.). The cooled mass was then decomposed with water (1 l.) and concentrated hydrochloric acid (500 ml.), and the mixture warmed to 80°. The precipitate crystallised from light petroleum (b. p. 100—120°) as bright red needles of the dione, m. p. 149° (9 g., 43%). It gave a dark green ferric chloride colour and dissolved in aqueous sodium carbonate. Light absorption: Max. at 216, 260, and 410 mμ (log ε 4·25, 3·9 and 3·92 respectively) in *cyclo*hexane. The dimethyl ether had max. at 214 and 330 mμ (log ε 4·29 and 3·55 respectively) in MeOH. The *oxime* of the dimethyl ether had m. p. 175° (from light petroleum) (Found: C, 62·3; H, 6·0; N, 5·35. $C_{13}H_{13}O_4N$ requires C, 62·6; H, 6·0; N, 5·6%).

Attempted Dehydrogenation of the Ether (II; R = OMe).—The dimethoxy-dione (2 g.) was refluxed in 1 : 2 : 4-trichlorobenzene (20 ml.) with palladised charcoal (2 g., 10%) for 11 hr. under nitrogen. The material soluble in aqueous sodium hydroxide (10%) crystallised from light petroleum (b. p. 100—120°) to give starting material, and, after concentration of the mother-liquor, the yellow *monomethyl ether*. The latter, separated from light petroleum (b. p.

80—90°), had m. p. 86° (Found: C, 65·0; H, 5·3; OMe, 13·35. $C_{12}H_{12}O_4$ requires C, 65·5; H, 5·45; OMe, 14·1%).

*4-Ethylidene-1′ : 4′-dimethoxy-1 : 2-benzo*cyclo*heptene-3 : 7-dione* (IV; R = Me).—To 1′ : 4′-dimethoxy-1 : 2-benzo*cyclo*heptene-3 : 7-dione (1 g.), dissolved in concentrated hydrochloric acid (60 ml.), was added acetaldehyde (0·3 g.). After 3 days, the orange precipitate was collected (0·7 g., 63%). Crystallisation from benzene–light petroleum (b. p. 100—120°) gave the dull yellow *ethylidene derivative*, m. p. 228° (Found: C, 69·1; H, 6·0. $C_{15}H_{16}O_4$ requires C, 69·25; H, 6·15%).

*4-Benzylidene-1′ : 4′-dimethoxy-1 : 2-benzo*cyclo*heptene-3 : 7-dione* (IV; R = Ph).—Freshly distilled benzaldehyde (0·4 g.) was added to the dimethoxy-dione (1 g.) in concentrated hydrochloric acid (60 ml.). Next day the yellow precipitate was collected and crystallised from glacial acetic acid (charcoal); the *product* was obtained as lemon-yellow needles, m. p. 204° (0·8 g., 58%) (Found: C, 74·35; H, 5·9. $C_{20}H_{16}O_4$ requires C, 74·5; H, 5·6%).

*4-Bromobenzyl(?)-1′ : 4′-dihydroxy-1 : 2-benzo*cyclo*heptene-3 : 7-dione* (VI).—To a solution of glacial acetic acid (35 ml.) saturated with anhydrous hydrogen bromide was added the benzylidene-dione (0·5 g.). The mixture was warmed at 60° for 11 hr., after which it was poured into water. The dull yellow precipitate was collected and crystallised from light petroleum (b.p. 100—120°) (charcoal) in yellow needles, m. p. 157° (100 mg.) (Found: C, 57·8; H, 3·9; Br, 20·3. $C_{18}H_{15}O_4Br$ requires C, 57·6; H, 4·0; Br, 21·3%). The mother liquor gradually deposited a second crop of yellow needles. Recrystallisation from light petroleum (b. p. 100—120°) gave lemon-yellow needles of an *isomer* (?) (70 mg.), m. p. 157° depressed on admixture with the previous compound (Found: C, 57·5; H, 3·9%). The first bromo-compound with methyl sulphate–potassium carbonate in boiling acetone gave 4-benzylidene-1′ : 4′-dimethoxy-1 : 2-benzo*cyclo*heptene-3 : 7-dione, m. p. and mixed m. p. 204°.

*4-Benzylidene-1′ : 4′-dihydroxy-1 : 2-benzo*cyclo*heptene-3 : 7-dione*—This was obtained from each of the above isomers, by dissolution in warm pyridine and, next day, pouring into dilute hydrobromic acid. The orange-yellow *product* was isolated by chloroform extraction and, crystallised from light petroleum (b. p. 100—120°), had m. p. 99° (Found: C, 73·7; H, 4·8. $C_{18}H_{14}O_4$ requires C, 73·5; H, 4·75%). Methylation gave the dimethyl ether, m. p. and mixed m. p. 204°.

*3-Acetoxy-1′ : 4′-dimethoxy-1 : 2-benzo*cyclo*hepta-1 : 3-diene-7-one*.—1′ : 4′-Dimethoxy-1 : 2-benzo*cyclo*heptene-3 : 7-dione (1 g.), *iso*propenyl acetate (2 ml.), and concentrated sulphuric acid (1 drop) were refluxed for 2 hr. Potassium acetate was added to neutralise the acid catalyst, and the mixture evaporated to dryness *in vacuo*. The solid residual *monoacetate* was washed with alcohol and crystallised from light petroleum (b. p. 100—120°) as feathery needles, m. p. 120° (1 g., 84%) (Found: C, 64·9; H, 5·85. $C_{15}H_{16}O_5$ requires C, 65·2; H, 5·8%). The *dienol acetate* was obtained by refluxing the monoacetate (1 g.) for 3·5 hr. with *iso*propenyl acetate (5 ml.) and concentrated sulphuric acid (1 drop), the acetone formed being allowed to distil off. It crystallised from light petroleum (b. p. 100—120°) in long needles, m. p. 151° (0·7 g., 60%) (Found: C, 64·1; H, 5·6. $C_{17}H_{16}O_6$ requires C, 64·2; H, 5·65%). This can also be obtained directly from the dimethoxy-dione (1; R = OMe) in 30% yield.

*1′ : 4′-Dimethoxy-1 : 2-benzo*cyclo*hepta-1 : 4-diene-3 : 7-dione*.—This was prepared from each of the above enol acetates by the same procedure. The acetate (2 g.) was dissolved in dry carbon tetrachloride (75 ml.) and *N*-bromosuccinimide (1 mol.) added. After refluxing about 2 hr., when a blue or violet colour developed, the mixture was cooled and the insoluble succinimide filtered off (the colour does not appear during the bromination of the monoenol acetate). Distillation of the solvent under reduced pressure left a dull yellow oil which was treated in one of two ways. (*a*) Addition of pyridine to dissolve the oil gave a deep red solution. After 12 hr., this mixture was poured into dilute hydrobromic acid, and the precipitate collected and crystallised from light petroleum (b. p. 80—90°), pale yellow crystals, m. p. 125°, being obtained (Found: C, 51·4; H, 4·1; Br, 22·2. $C_{15}H_{15}O_5Br$ requires C, 50·75; H, 4·2; Br, 22·5%). Subsequent treatment of this compound as in (*b*) gave the final product in low yield. (*b*) The oil from the bromination was dissolved in methanolic potassium hydroxide (25 ml.; 5%) and warmed gently on the steam-bath for 30 min. The mixture was then cooled, poured into water, and acidified with dilute hydrochloric acid, and the resulting suspension extracted with chloroform and dried ($MgSO_4$). Hot light petroleum (b. p. 100—120°) was then added to the chloroform solution, and most of the latter solvent boiled off. When the solution had cooled it was decanted from a little sticky material and then concentrated to turbidity. On cooling, the *diketone* separated in clusters of orange crystals. Recrystallisation from light petroleum gave yellow material, m. p. 163—164° (37% from the dienol acetate, 17% from the monoenol acetate)

(Found : C, 67·0; H, 5·25. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·15%). Light absorption : Max. at 208, 225 (inflection), and 370 mμ (log ε 4·38, 4·13, and 3·72 respectively) in MeOH. The *dioxime* decomposed at *ca.* 300—310° (crystals from dimethylformamide) (Found : C, 59·4; H, 5·5; N, 10·4. $C_{13}H_{14}O_4N_2$ requires C, 59·5; H, 5·4; N, 10·7%). The diketone (0·1 g.) was hydrogenated over Adams catalyst in glacial acetic acid (5 ml.). Hydrogen (1 mol.) was absorbed in 10 min. and the reaction was then stopped. The solvent was removed *in vacuo* and the residue crystallised from light petroleum (b. p. 100—120°) to give 1′ : 4′-dimethoxy-1 : 2-benzo*cyclo*heptene-3 : 7-dione as colourless prisms, m. p. and mixed m. p. 149°.

We are indebted to Mr. M. St. C. Flett for the infrared data. One of us (A. J. S. S.) thanks the Carnegie Trust for the Universities of Scotland for a scholarship and the University of Aberdeen for a research studentship during the tenure of which the work in this and the following two papers was carried out.

THE UNIVERSITY, OLD ABERDEEN, SCOTLAND. [*Received, February 24th*, 1955.]

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*Hydroxybenzotropones. Part II.** *The Isomeric* 1 : 2 : 3 : 4-*Tetrahydro*-2 : 3-*methylene*-1 : 4-*dioxonaphthalenes.*

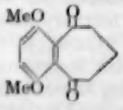
By A. J. S. SORRIE and R. H. THOMSON.

[Reprint Order No. 6172.]

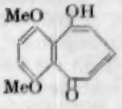
Bromination of diketones of type (I) and treatment of the products with pyridine gives *cyclo*propano-diketones of the type (III). The structure (III; R = Br) is established by hydrogenation, degradation, and spectroscopic evidence.

Bromomethylnaphthaquinones can be prepared by reaction of the corresponding methylnaphthaquinones with *N*-bromosuccinimide.

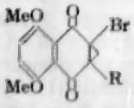
ONE of the unsuccessful procedures used in efforts to convert the ether (I) into the hydroxybenzotropone (II) was bromination–dehydrobromination (see Part I *). This led to a number of bromo-compounds isomeric with the desired hydroxybenzotropones. The structures of these compounds are now considered.



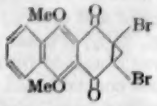
(I)



(II)



(III)



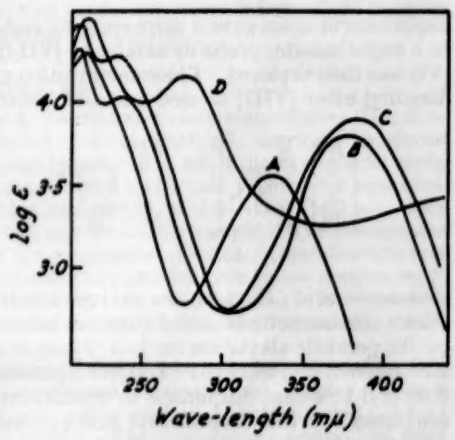
(IV)

Bromination of the ether (I) with 2 mols. of bromine in glacial acetic acid gave a dibromo-derivative which on treatment with pyridine lost the elements of hydrogen bromide to give a pale yellow, alkali-insoluble product, $C_{13}H_{11}O_4Br$. The same substance was obtained in lower yield by using *N*-bromosuccinimide, but we were unable to produce a bromine-free compound. Similarly, use of 4 mols. of bromine led to an unstable tetrabromo-diketone which lost bromine when treated with pyridine to yield a second yellow, alkali-insoluble compound, $C_{13}H_{10}O_4Br_2$. The two products were obviously closely related (the ultraviolet absorption curves are annexed) and, since dehydrogenation had occurred in their formation from the ether (I), they were regarded as (III; R = H and Br). This has now been established. Debromination with pyridine, referred to above, appears to be new but an analogous reaction was observed by Ingold (*J.*, 1921, **119**, 305) who found that reaction of αα′-dibromoglutaric ester with alcoholic potassium hydroxide gave a mixture in which bromine-free *cyclo*propane derivatives predominated. Reaction of the phenol (I; OH in place of OMe) with 2 mols. of bromine gave two bromo-derivatives. Treated separately with pyridine they afforded a mono- and a di-bromodihydroxy-diketone from which the compounds (III; R = H and Br) were obtained by methylation. The dibromo-diketone (III; R = Br) was examined in detail.

* Part I, preceding paper.

Determination of Structure.—The bromine atoms. As the bromine atoms in the compound (III; R = Br) were completely stable to alkaline hydrolysis they could either be at bridgehead positions (as shown) or be located *ortho* to the methoxyl groups. By condensing glutaric acid with 2 : 3-dichloro- and with 2 : 3-dimethyl-quinol, and methylation of the products, two further diketones of type (I), but having positions 6 and 7 blocked, were obtained. Bromination of these diketones with 4 mols. of bromine and treatment with pyridine again yielded dibromo-compounds in which the bromine atoms must be attached to the α-carbon atoms. Structure (III) therefore appeared to be correct as far as the bromine atoms were concerned. Some further evidence is mentioned below.

The cyclo*propane ring.* The existence of the *cyclo*propane ring was demonstrated by reactions in which the ring was opened in both possible ways. Catalytic hydrogenation over Adams catalyst led to ring fission and removal of the bromine atoms. After uptake of 3 mols. of hydrogen the original diketone (I) was isolated. Reaction of the compound (III; R = Br) with hydrobromic acid in boiling acetic acid resulted in opening of the *cyclo*propane ring and demethylation to a product $C_{11}H_6O_4Br_2$. A closely related substance



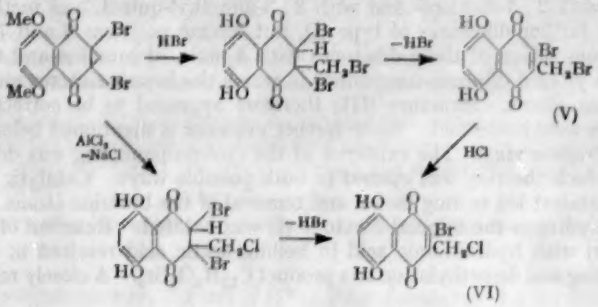
A, 1′ : 4′-*Dimethoxy*-1 : 2-*benzo*cyclo*heptene*-3 : 7-*dione* (I).
B, 2-*Bromo*-1 : 2 : 3 : 4-*tetrahydro*-5 : 8-*dimethoxy*-2 : 3-*methylene*-1 : 4-*dioxonaphthalene* (III; R = H).
C, 2 : 3-*Dibromo*-1 : 2 : 3 : 4-*tetrahydro*-5 : 8-*dimethoxy*-2 : 3-*methylene*-1 : 4-*dioxonaphthalene* (III; R = Br).
D, *Bromonaphthazarin dimethyl ether* (VIII).

Solvent: methanol.

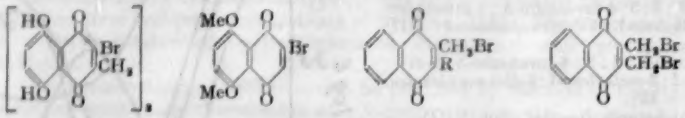
$C_{11}H_6O_4BrCl$, was obtained by fusion in sodium chloride–aluminium chloride at 180°. The latter product was also obtained by refluxing the former in hydrochloric–acetic acid. Mixed melting point determinations of the two compounds showed no depression; this was also true of their diacetates. The compounds were readily recognised as naphthazarins by their deep cornflower-blue solutions in aqueous sodium hydroxide and sodium carbonate, by the formation of diacetates but not methyl ethers, and by their light absorption. The formula $C_{11}H_6O_4Br_2$ corresponds to a dibromomethylnaphthazarin. If the initial bromination of the ether (I) had taken place partly in the benzenoid ring a reasonable structure for this product would be 6 : 7-dibromo-2-methylnaphthazarin. This was synthesised by the condensation of dibromomaleic anhydride with toluquinol. The two compounds were different although their ultraviolet absorption spectra were very similar. This further established the location of the bromine atoms in the compound (III; R = Br). The most probable formulation of this new dibromonaphthazarin therefore seemed to be 2-bromo-3-bromomethylnaphthazarin (V) which could arise as shown.

Reduction of the quinone (V) to 2-bromo-3-methylnaphthazarin would be a convenient way to establish its structure. It has been shown (Thomson, *J.*, 1953, 1196) that catalytic reduction of chloromethylnaphthaquinones at a palladium catalyst gives rise (after reoxidation) to diquinones, but we now find that use of a platinum catalyst leads to the corresponding methylquinone, *e.g.*, 2-chloromethyl-3-methyl-1 : 4-naphthaquinone reduced with hydrogen and Adams catalyst and then reoxidised gave 2 : 3-dimethyl-1 : 4-naphthaquinone. However this procedure was not successful with the compound (V); the product

was not 2-bromo-3-methylnaphthazarin but an unidentified naphthazarin of high m. p. and low solubility, probably another diquinone (VII?). Reduction by the stannous chloride method (Bruce and Thomson, *J.*, 1952, 2759) to obtain a simple β-hydro-



naphthazarin again gave a more complex compound of high m. p. which could be oxidised to a naphthazarin, probably similar to (VII?). Direct synthesis of the quinones (V) and (VI) was then explored. Chloromethylation and bromomethylation of bromonaphthazarin dimethyl ether (VIII) seemed a feasible route but reaction in formaldehyde–hydrochloric



acid–acetic acid (Thomson, *loc. cit.*) gave only a little 2 : 3-dichloronaphthazarin dimethyl ether. Bromomethylation of quinones has only been achieved hitherto in very low yield by the peroxide alkylation method (Fieser *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 3203), but 2-bromomethyl-3-methyl-1 : 4-naphthaquinone (IX; R = Me) was readily obtained from 2-methyl-1 : 4-naphthaquinone in formaldehyde–hydrobromic acid–acetic acid, and was converted into the chloromethyl analogue with hydrochloric acid. We could not extend this procedure to the bromomethylation of the quinone (VIII) and Kubiezek and Neugebauer's method (*Monatsh.*, 1950, **81**, 917) was also unsuccessful. The failure to bromomethylate and chloromethylate bromo(and chloro)naphthazarin dimethyl ether is probably due to salt formation with the halogen acid (Bruce and Thomson, *J.*, 1955, 1089). Finally a general synthesis of bromomethylnaphthaquinones was found in the reaction of methylnaphthaquinones with *N*-bromosuccinimide. In this way the compounds (IX; R = H and Br) were obtained from 2-methyl- and 3-bromo-2-methyl-1 : 4-naphthaquinone; and 2 : 3-dimethyl-1 : 4-naphthaquinone afforded the dibromide (X). The reaction failed with methylnaphthazarin, but 2-bromo-3-methylnaphthazarin diacetate yielded 2-bromo-3-bromomethylnaphthazarin diacetate, hydrolysis of which gave the desired dibromoquinone (V). This established the structure (V) and hence (III; R = Br). The structure (VI) for the bromochloro-product obtained by aluminium chloride degradation of the compound (III; R = Br) is based on the fact that it can be obtained from the dibromo-compound (V) by reaction with hydrochloric acid in acetic acid; and the monobromo-compound (IX; R = Me) also gives the corresponding chloromethyl compound under the same conditions, whereas 3-bromo-2-methylnaphthazarin is unaffected.

Spectroscopic evidence. Infrared examination of the compounds (III; R = Br) and (IV) supported the chemical evidence described above. No infrared spectra for *cyclo*propane compounds of this complexity are available but from an examination of many simpler compounds, including *cyclo*propano-ketones, Slabey (*J. Amer. Chem. Soc.*, 1954, **76**, 3604) has shown that a band in the 9·5—10·0-μ region is characteristic of a *cyclo*propane ring. The diketone (III; R = Br) showed absorption bands at 988 and 1058 cm.$^{-1}$, and

the analogue (IV) at 990 and 1032 cm.$^{-1}$, but this is not reliable evidence of the existence of a *cyclo*propane ring in these compounds since the diketone (I) shows a weak band at 990 cm.$^{-1}$ and stronger bands at 1016, 1045, and 1060 cm.$^{-1}$, and absorption in this region appears to be general for such *peri*-methoxy cyclic ketones (unpublished work). The infrared spectra of a number of organic bromides have been examined in the 14·5—19·5-μ region by Mortimer, Blodgett, and Daniels (*J. Amer. Chem. Soc.*, 1947, **69**, 822) who found that aliphatic bromides showed two bands, one in the region 515—570 cm.$^{-1}$, the other in the region 645—690 cm.$^{-1}$; the three aliphatic dibromides studied showed no characteristic C–Br bands outside the range 554—652 cm.$^{-1}$. Bromobenzene and α-bromonaphthalene give bands at 678 and 648 cm.$^{-1}$ respectively. The diketone (III; R = Br) shows two bands in this region, one at 551 and the other at 700 cm.$^{-1}$ (which seems too high for a C–Br vibration), and the compound (IV) gives a band at 576 cm.$^{-1}$. From this it appears that the two bromine atoms in both compounds are attached to the aliphatic ring in agreement with the chemical evidence.

These compounds also exemplify the ability of *cyclo*propane rings to conjugate with neighbouring double bonds. This is seen in the appearance of colour on passing from (I) to (III) and the shift in the ultraviolet absorption produces a curve intermediate between those of (I) and bromonaphthazarin dimethyl ether (see Figure).

Experimental

2-*Bromo*-1 : 2 : 3 : 4-*tetrahydro*-5 : 8-*dimethoxy*-2 : 3-*methylene*-1 : 4-*dioxonaphthalene* (III; R = H).—To 1′ : 4′-dimethoxy-1 : 2-benz*ocyclo*heptene-3 : 7-dione (1·17 g.), dissolved in glacial acetic acid (10 ml.), was added slowly with stirring, bromine (0·53 ml., 2 mols.) in glacial acetic acid (2 ml.). Evolution of hydrogen bromide soon started and a pale yellow solid separated. After 5 hr., the dibromo-derivative was collected and had m. p. 168—170° (1·82 g.). This product (1 g.) was dissolved in hot pyridine (8 ml.) and set aside overnight. The mixture was then poured into dilute hydrobromic acid, and the precipitate collected. Crystallisation first from aqueous acetic acid and then from benzene (charcoal) afforded pale yellow needles, m. p. 208° (decomp.) (0·7 g., 88%) (Found: C, 50·5; H, 3·7; Br, 25·8. $C_{13}H_{11}O_4Br$ requires C, 50·15; H, 3·55; Br, 25·75%). Light absorption: max. at 210, 235, and 380 mμ (log ε 4·32, 4·03, and 3·79 respectively) in MeOH.

2 : 3-*Dibromo*-1 : 2 : 3 : 4-*tetrahydro*-5 : 8-*dimethoxy*-2 : 3-*methylene*-1 : 4-*dioxonaphthalene* (III; R = Br).—The procedure was the same as above except that bromine (1·1 ml., 4 mols.) was used. The intermediate tetrabromo-derivative was a bright yellow solid, m. p. 224° (decomp.) (2·5 g.) (Found: Br, 56·0. $C_{13}H_{10}O_4Br_4$ requires Br, 58·0%). The final *product* crystallised from benzene (charcoal) in bright yellow needles, m. p. 251° (decomp.) (0·8 g., 45%) (Found: C, 39·7; H, 2·7; Br, 40·2. $C_{13}H_{10}O_4Br_2$ requires C, 40·0; H, 2·55; Br, 41·0%). Light absorption: max. at 210, 232, and 383 mμ (log ε 4·48, 4·26, and 3·90 respectively) in MeOH.

2-*Bromo*-1 : 2 : 3 : 4-*tetrahydro*-5 : 8-*dihydroxy*-2 : 3-*methylene*-1 : 4-*dioxonaphthalene*.—Bromine (1·1 ml., 4 mols.) in glacial acetic acid (2 ml.) was added with stirring to a solution of 1′ : 4′-dihydroxy-1 : 2-benz*ocyclo*heptene-3 : 7-dione (1 g.) in the same solvent (30 ml.). After 5 days, the yellow crystals which had separated were collected (m. p. 186°). Dilution of the filtrate with water afforded a red precipitate (m. p. 50°). The solid, m. p. 186°, was dissolved in hot pyridine (5 ml.), set aside for 12 hr., then poured into dilute hydrobromic acid, and the precipitate crystallised from benzene–light petroleum (b. p. 80—90°) to give the *bromo-derivative* as yellow needles, m. p. 135° (Found: C, 46·75; H, 2·45; Br, 28·1. $C_{11}H_7O_4Br$ requires C, 46·65; H, 2·45; Br, 28·3%). The bromo-derivative, m. p. 50°, gave, after the same treatment with pyridine, **2 : 3-*dibromo*-1 : 2 : 3 : 4-*tetrahydro*-5 : 8-*dihydroxy*-2 : 3-*methylene*-1 : 4-*dioxonaphthalene***, as orange-yellow needles, m. p. 174° (from light petroleum, b. p. 100—120°) (Found: C, 36·65; H, 1·7; Br, 43·8. $C_{11}H_6O_4Br_2$ requires C, 36·45; H, 1·65; Br, 44·2%). Methylation of these two compounds with methyl sulphate–acetone–potassium carbonate afforded the respective dimethyl ethers (III; R = H and Br).

1′ : 4′-*Dihydroxynaphtho*(2′ : 3′-1 : 2)cyclo*heptene*-3 : 7-*dione*.—The **p-*nitrophenylhydrazone*** crystallised from aqueous acetic acid in orange crystals, m. p. 228° (Found: C, 64·15; H, 4·75; N, 10·8. $C_{31}H_{17}O_5N_3$ requires C, 64·45; H, 4·35; N, 10·8%).

2 : 3-*Dibromo*-1 : 2 : 3 : 4-*tetrahydro*-9 : 10-*dimethoxy*-2 : 3-*methylene*-1 : 4-*dioxoanthracene* (IV).—To 1′ : 4′-dimethoxynaphtho(2′ : 3′-1 : 2)*cyclo*heptene-3 : 7-dione (0·14 g.), dissolved in glacial acetic acid (7 ml.), was added bromine (0·05 ml.) in the same solvent (1 ml.). After 6 days, the

solution was diluted with water, and the precipitate collected (m. p. 80°). Treatment with pyridine, as described above, gave the *product* as pale yellow needles, m. p. 147° (from aqueous methanol) (70 mg.) (Found : C, 46·6; H, 3·0. $C_{17}H_{12}O_4Br_2$ requires C, 46·35; H, 2·75%).

2′ : 3′-Dichloro-1′ : 4′-dihydroxy-1 : 2-benzocycloheptene-3 : 7-dione.—This was prepared from 2 : 3-dichloroquinol and glutaric acid by the procedure of Bruce, Sorrie, and Thomson (*J.*, 1953, 2403). The *diketone* crystallised from light petroleum (b. p. 100—120°) in orange-yellow leaflets, m. p. 204° (16%). Sublimation *in vacuo* gave bright yellow crystals (Found : C, 48·0; H, 3·05; Cl, 25·5. $C_{11}H_8O_4Cl_2$ requires C, 48·0; H, 3·0; Cl, 25·8%). The *dimethyl ether* crystallised from aqueous acetic acid in needles, m. p. 135° (Found : C, 51·3; H, 4·15. $C_{13}H_{12}O_4Cl_2$ requires C, 51·15; H, 3·95%).

2 : 3-Dibromo-6 : 7-dichloro-1 : 2 : 3 : 4-tetrahydro-5 : 8-dimethoxy-2 : 3-methylene-1 : 4-dioxonaphthalene.—Bromination of the above dimethyl ether with bromine (4 mols.) gave a solid, m. p. 178—180°. Treatment with pyridine gave the desired *product* which crystallised from light petroleum (b. p. 80—90°) in pale yellow, slender, needles, m. p. 211° (decomp.) (Found : C, 34·1; H, 1·55. $C_{13}H_8O_4Br_2Cl_2$ requires C, 34·0; H, 1·75%).

1′ : 4′-Dihydroxy-2′ : 3′-dimethyl-1 : 2-benzocycloheptene-3 : 7-dione.—This *diketone*, prepared from 2 : 3-dimethylquinol and glutaric acid, crystallised from light petroleum (b. p. 100—120°), forming orange needles, m. p. 83° (34%) (Found : C, 66·3; H, 5·9. $C_{13}H_{14}O_4$ requires C, 66·6; H, 6·0%). The *dimethyl ether* crystallised from light petroleum (b. p. 100—120°) in cream-coloured rosettes, m. p. 84° (Found : C, 68·55; H, 6·8. $C_{15}H_{18}O_4$ requires C, 68·7; H, 6·9%).

2 : 3-Dibromo-1 : 2 : 3 : 4-tetrahydro-5 : 8-dimethoxy-6 : 7-dimethyl-2 : 3-methylene-1 : 4-dioxonaphthalene.—The initial bromination *product* had m. p. 145°. Treatment of this with pyridine afforded an oily solid which was washed with ether and then crystallised from light petroleum (b. p. 100—120°) to give stout needles, m. p. 165° (47%) (Found : C, 42·95; H, 3·35; Br, 37·9. $C_{15}H_{14}O_4Br_2$ requires C, 43·05; H, 3·35; Br, 38·3%).

Reactions of 2 : 3-Dibromo-1 : 2 : 3 : 4-tetrahydro-5 : 8-dimethoxy-2 : 3-methylene-1 : 4-dioxonaphthalene.—(a) *Hydrogenation.* The dione (1 g.), dissolved in glacial acetic acid, was hydrogenated over Adams catalyst (50 mg.). After the absorption of 3 mols. of hydrogen, the catalyst was filtered off and the solvent evaporated under reduced pressure. The oily residue solidified on drying *in vacuo* and was crystallised from light petroleum (b. p. 100—120°) to give 1′ : 4′-dimethoxy-1 : 2-benzocycloheptene-3 : 7-dione (0·35 g.), m. p. and mixed m. p. 149°.

(b) *With hydrobromic acid.* To a boiling solution of the dione (0·5 g.) in glacial acetic acid (20 ml.), was added hydrobromic acid (3 ml.; 48%). After being heated for 20 min.—the colour had changed to deep violet—the mixture was poured into water and the precipitate collected. Crystallisation from light petroleum (b. p. 100—120°) gave brown, lustrous plates of *2-bromo-3-bromomethylnaphthazarin*, m. p. 149° (0·15 g.) (Found : C, 36·2; H, 1·6; Br, 44·3. $C_{11}H_6O_4Br_2$ requires C, 36·45; H, 1·65; Br, 44·0%). The *diacetate* crystallised from light petroleum (b. p. 100—120°) as maroon crystals, m. p. 206° (Found : C, 39·7; H, 2·2; Br, 35·9. $C_{15}H_{10}O_6Br_2$ requires C, 39·5; H, 2·2; Br, 35·9%).

(c) *With fused sodium chloride–aluminium chloride.* To a molten mixture of sodium chloride (3 g.) and anhydrous aluminium chloride (12 g.) at 140° was added the dione (0·7 g.). After being heated for 2 min. at 180° the mixture was cooled and decomposed with dilute hydrochloric acid (180 ml.; 2 : 1). The precipitate was collected and crystallised from light petroleum (b. p. 100—120°) to give *2-bromo-3-chloromethylnaphthazarin* as dark needles with a green sheen, m. p. 154° (0·32 g.) (Found : C, 41·85; H, 2·0; Hal, 36·1. $C_{11}H_6O_4BrCl$ requires C, 41·6; H, 1·9; Hal, 36·4%). This product was also obtained by passing a stream of dry hydrogen chloride through a refluxing solution of 2-bromo-3-bromomethylnaphthazarin in glacial acetic acid for 6 hr. The *diacetate* crystallised from light petroleum (b. p. 100—120°) in orange crystals, m. p. 199° (Found : C, 44·75; H, 2·75; Hal, 27·8. $C_{15}H_{10}O_6BrCl$ requires C, 44·85; H, 2·5; Hal, 28·8%).

6 : 7-Dibromo-2-methylnaphthazarin.—This *quinone* was prepared by condensation of toluquinol and dibromomaleic acid in molten sodium chloride–aluminium chloride. Crystallisation from light petroleum (b. p. 100—120°) afforded golden-brown plates, m. p. 160° (27%) (Found : C, 36·35; H, 1·6; Br, 43·5. $C_{11}H_6O_4Br_2$ requires C, 36·45; H, 1·65; Br, 44·0%). Reduction with acid stannous chloride gave β-hydromethylnaphthazarin, m. p. and mixed m. p. 160° (Bruce and Thomson, *loc. cit.*).

Reduction of 2-Chloromethyl-3-methyl-1 : 4-naphthaquinone.—The quinone (0·5 g.), dissolved in glacial acetic acid (15 ml.), was hydrogenated over Adams catalyst (0·1 g.). After the absorption of 2 mols. of hydrogen, the catalyst was filtered off and washed with hot solvent.

To the combined filtrates a solution of chromium trioxide (0·2 g.) in water (2 ml.) was added, and the mixture heated for 20 min. on a steam-bath and poured into water. The yellow precipitate crystallised from aqueous acetic acid in lemon-yellow needles of 2 : 3-dimethyl-1 : 4-naphthaquinone (0·25 g.), m. p. and mixed m. p. 120°.

2-Bromomethyl-3-methyl-1 : 4-naphthaquinone.—A solution of 2-methyl-1 : 4-naphthaquinone (3 g.), acetic acid (35 ml.), and formaldehyde (9 ml.; 36%) was coooled to 0° and a stream of hydrogen bromide passed through it for 45 min. The solution became red and a solid separated. Next morning the solid was collected and crystallised from ethanol in yellow needles, m. p. 131° (43%) (Fieser *et al., loc. cit.*, report m. p. 134°) (Found : Br, 30·2. Calc. for $C_{12}H_9O_2Br$: Br, 30·2%). This quinone (1 g.) in glacial acetic acid (20 ml.) and concentrated hydrochloric acid (10 ml.) was refluxed for 1 hr., concentrated hydrochloric acid (5 ml.) added, and the mixture refluxed for a further 30 min. and poured into water. The precipitate crystallised from aqueous alcohol in yellow needles, m. p. 106°, undepressed on admixture with 2-chloromethyl-3-methyl-1 : 4-naphthaquinone.

2-Bromonaphthazarin Dimethyl Ether.—To naphthazarin dimethyl ether (1 g.) in glacial acetic acid was added bromine (0·9 g.) in the same solvent (2 ml.). After 30 min. sodium acetate (0·5 g.) was added, and the mixture refluxed for 20 min. and poured into water. The precipitate was crystallised first from alcohol (charcoal) and then from light petroleum (b. p. 100—120°) to give orange-red needles of the *bromo-compound*, m. p. 160° (0·7 g., 50%) (Found : C, 48·9; H, 3·1; Br, 27·0. $C_{12}H_9O_4Br$ requires C, 48·5; H, 3·05; Br, 26·9%). Attempted chloromethylation of this product gave 2 : 3-*dichloronaphthazarin dimethyl ether*, orange-red needles, m. p. 237° (from alcohol). This was also obtained as follows : dry chlorine (0·15 g.) was passed into a solution of naphthazarin dimethyl ether (0·25 g.) in glacial acetic acid (10 ml.). The solution was heated for 15 min. on the steam-bath (HCl evolution), cooled, and diluted with water (50 ml.) and the scarlet precipitate collected and crystallised from alcohol. It had m. p. and mixed m. p. 237° (Found : C, 50·4; H, 2·8; Cl, 24·3. $C_{12}H_8O_4Cl_2$ requires C, 50·2; H, 2·8; Cl, 24·7%). Demethylation with sodium chloride–aluminium chloride gave 2 : 3-dichloronaphthazarin, m. p. and mixed m. p. 192° (diacetate, m. p. and mixed m. p. 231°).

2-Bromo-3-methylnaphthazarin.—Bromine (0·2 ml.) was added to a solution of 2-methylnapthazarin diacetate (1 g.) in glacial acetic acid (25 ml.). After 4 days sodium acetate was added and the mixture refluxed for 20 min., before dilution with water. The precipitate crystallised from light petroleum (b. p. 100—120°), to give the orange *bromo-diacetate*, m. p. 197° (0·9 g.) (Found : C, 49·2; H, 3·05; Br, 21·6. $C_{16}H_{11}O_6Br$ requires C, 49·05; H, 3·0; Br, 21·8%). The diacetate (0·5 g.) was refluxed for 1 hr. with concentrated hydrochloric acid (10 ml.), the mixture diluted with water, and the precipitate collected and crystallised from light petroleum (b. p. 80—90°) (charcoal) to give 2-*bromo-3-methylnaphthazarin* as slender, crimson needles, m. p. 193° (0·2 g.) (Found : C, 46·8; H, 2·6; Br, 28·5. $C_{11}H_7O_4Br$ requires C, 46·65; H, 2·45; Br, 28·3%).

Bromination of Methyl-1 : 4-naphthaquinones.—General procedure. To the quinone, dissolved in dry carbon tetrachloride, was added *N*-bromosuccinimide (1 or 2 mols. as required) and a trace of benzoyl peroxide. The mixture was refluxed for 16—20 hr., the insoluble succinimide was filtered off after cooling, and the solvent removed, leaving the product. Thus 3-*bromo*-2-*bromomethyl*-1 : 4-*naphthaquinone* was prepared from 3-bromo-2-methyl-1 : 4-naphthaquinone; it crystallised from methanol in yellow needles, m. p. 119° (Found : C, 40·0; H, 1·5; Br, 48·8. $C_{11}H_6O_2Br_2$ requires C, 40·0; H, 1·8; Br, 48·5%). 2-*Bromomethyl*-1 : 4-*naphthaquinone*, from 2-methyl-1 : 4-naphthaquinone, crystallised from methanol in orange-yellow needles, m. p. 98°, which slowly darken (Found : C, 52·1; H, 2·75; Br, 30·6. $C_{11}H_7O_2Br$ requires C, 52·5; H, 2·8; Br, 31·8%). 2 : 3-Dimethyl-1 : 4-naphthaquinone afforded 2 : 3-*bisbromomethyl*-1 : 4-*naphthaquinone* (long, yellow needles from ethanol), m. p. 154° (Found : C, 41·6; H, 2·5; Br, 46·0. $C_{12}H_8O_2Br_2$ requires C, 41·9; H, 2·3; Br, 46·4%). The bromination of 2-bromo-3-methylnaphthazarin diacetate required 36 hr. 2-Bromo-3-bromomethylnaphthazarin diacetate was obtained and had m. p. 192°, raised to 196° on admixture with a sample prepared as previously described. Hydrolysis gave 2-bromo-3-bromomethylnaphthazarin, m. p. and mixed m. p. 149°. Re-acetylation afforded the diacetate, m. p. and mixed m. p. 205°.

We thank Dr. T. S. Robinson for the infrared data, and Coalite and Chemical Products Ltd. for a gift of 2 : 3-dimethylphenol.

THE UNIVERSITY, OLD ABERDEEN. [*Received, February 24th*, 1955.]

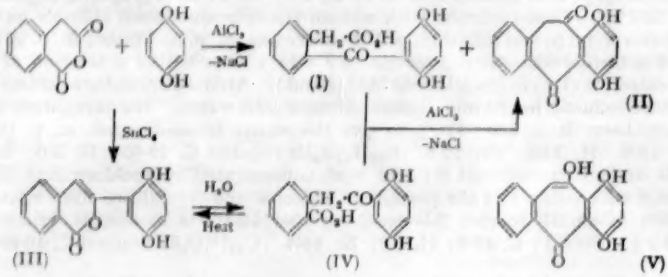
Hydroxybenzotropones. Part III. Synthesis of a Hydroxydimethoxydibenzotropone.*

By A. J. S. Sorrie and R. H. Thomson.

[Reprint Order No. 6173.]

The dimethoxy-1 : 2 : 4 : 5-dibenz*ocyclo*heptadienedione (VI) has been obtained *via* a condensation of quinol with homophthalic anhydride. It behaves as an enol-ketone, showing no tropolone characteristics.

In the condensation of quinol and glutaconic acid (see Part I *) the intermediate keto-acid cyclises to a five-membered ring, forming an oxoindanylacetic acid. When homophthalic acid (the aromatic analogue of glutaconic acid) is used a similar ring closure is prohibited and conditions are more favourable for the formation of a seven-membered ring. Thus condensation of homophthalic acid (or anhydride) with quinol in molten sodium chloride–aluminium chloride gave the dione (II) in low yield, and a small amount of the keto-acid (I) which was converted into the dione on further treatment in the fusion mixture. A Friedel–Crafts reaction between homophthalic anhydride and quinol in stannic chloride (Buu-Hoï, *Bull. Soc. chim. France*, 1944, **11**, 338) gave the *iso*coumarin (III) which was readily hydrolysed to the keto-acid (IV), isomeric with (I). This acid (IV) is reconverted into the *iso*coumarin when heated, or when dissolved in anhydrous hydrofluoric acid, but on fusion in sodium chloride–aluminium chloride again yields the dione (II).

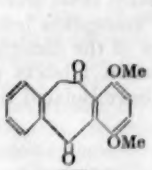


The orange dione (II) forms a diacetate and a trimethyl ether with methyl sulphate, but is not methylated by diazomethane. It also reacts with phenylhydrazine although the product is not a simple hydrazone. It gives a green ferric chloride colour but no colour with boroacetic anhydride, and is extracted from chloroform by a solution of pH 9·8. It forms an orange-red solution in cold aqueous sodium hydroxide and dissolves in hot aqueous sodium carbonate; it is reduced in alkaline solution by sodium dithionite but the addition of hydrogen peroxide does not restore the colour. The infrared spectrum shows that this compound exists as the dione (II) rather than as the hydroxytropone (V). In the 6-μ region there is a strong band at 1640 cm.$^{-1}$ and a very strong band at 1600 cm.$^{-1}$, indicating the presence of two unsymmetrical strongly hydrogen-bonded carbonyl groups. In the 3-μ region there is a broad band at 3000 cm.$^{-1}$ and two sharp but weak bands at 2997 and 3050 cm.$^{-1}$. The last two are most probably due to aromatic C–H vibrations. There is no band near 3300 cm.$^{-1}$. All this is in favour of structure (II) but not (V). Moreover the spectrum showed no significant change in carbon tetrachloride solution, showing the hydrogen-bonding to be almost all intramolecular. Some resemblance to quinizarin (1 : 4-dihydroxyanthraquinone) in physical properties might therefore be expected. This is seen again in the ultraviolet absorption where the curve of the diketone (II) is similar in character to that of quinizarin (see Morton and Earlam, *J.*, 1941, 159; Spruit, *Rec. Trav.*

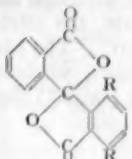
* Parts I and II, the two preceding papers.

chim., 1949, **68**, 325), the maxima in the latter case falling at longer wavelengths as would be expected from the more extended conjugation.

The trimethyl ether (V; OMe in place of OH) is completely stable to alkaline hydrolysis but under acid conditions it gave the dimethyl ether (VI). This is slightly soluble in



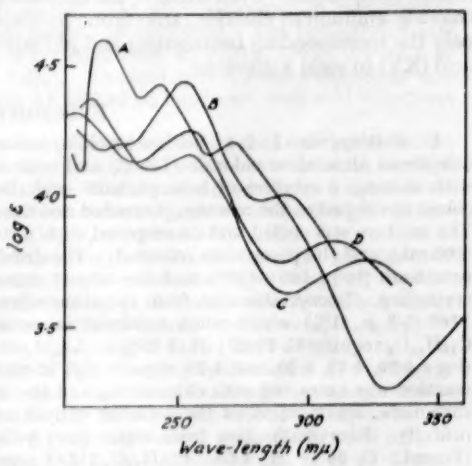
(VI)



(VII)

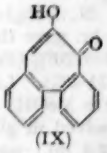
(VIII)

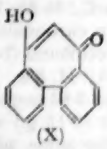
concentrated hydrochloric acid, and soluble in hot caustic alkalis, forming an orange solution, and gives no ferric colour. It formed a 2 : 4-dinitrophenylhydrazone and a 3 : 5-dinitrobenzoate, and reaction with methyl sulphate regenerated the trimethyl ether.

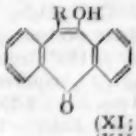


A, 1′ : 4′-*Dihydroxy*-1 : 2-4 : 5-*dibenzo*cyclo-*heptadiene*-3 : 7-*dione* (II).
B, *Diacetate of* (*A*).
C, *Dimethyl ether* (VI) *of* (*A*).
D, *Trimethyl ether of* (*A*).
Solvent: methanol.

Oxidation of the trimethyl ether with sodium dichromate in acetic acid gave a colourless product, insoluble in hot sodium carbonate solution but dissolving in warm dilute aqueous sodium hydroxide; the original compound was obtained by acidification of the alkaline solution. Quantitative hydrolysis showed the presence of two lactone rings and the oxidation product is considered to be (VII; R = OMe). This is supported by a carbonyl band in the infrared spectrum at the unusually high value of 1787 cm.$^{-1}$; Grove (*J.*, 1952, 3345) found the carbonyl band in 3-acetoxyphthalides to be as high as 1785 cm.$^{-1}$. The


(IX)

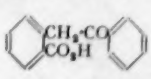

(X)


(XI; R = H)
(XII; R = Ph)

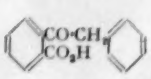
dilactone (VII; R = H) was obtained by Treibs and Klinkhammer (*Ber.*, 1951, **84**, 671) from dibenzotropone (VIII) on ozonolysis and oxidation of the aldehydo-acid obtained.

It can now be seen that the diketone (II) and its dimethyl ether (VI), like all the other known hydroxydibenzotropones [(IX), Nakasaki, *J. Chem. Soc. Japan*, 1951, **72**, 739;

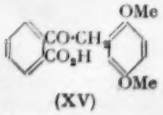
(X), Lucien and Taurins, *Canad. J. Chem.*, 1952, **30**, 208; (XI), Rigaudy and Nedelec, *Compt. rend.*, 1953, **237**, 1097; (XII), Cook, *J.*, 1928, 58], show no characteristic tropolone properties. They behave as enol-ketones. The dimethyl ether of the diketone (II) is the least acidic of the group. This may be due to suppression of enolisation by the *peri*-methoxyl groups (see Part I, *loc. cit.*), although the dimethyl ether seems to exist, at least in methanol solution, in the enol form, the ultraviolet absorption being very similar to that of the trimethyl ether (see Figure). The enol form of the dimethyl ether would be slightly stabilised by hydrogen-bonding whereas chelation inhibits enolisation of the diketone (II). Rigaudy and Nedelec (*loc. cit.*) claim to have isolated the hydroxytropone (XI) in both enol and keto-forms.



(XIII)



(XIV)



(XV)

After the synthesis of the diketone (II) some further experiments were made to obtain related compounds. Cyclisation of the keto-acids (XIII) and (XIV) by use of fused sodium chloride–aluminium chloride, anhydrous hydrogen fluoride, and polyphosphoric acid gave only the corresponding *iso*coumarin and phthalide. More surprising was the failure of the acid (XV) to yield a diketone.

Experimental

1′ : 4′-*Dihydroxy*-1 : 2-4 : 5-*dibenzo*cyclo*heptadiene*-3 : 7-*dione* (II).—To a molten mixture of anhydrous aluminium chloride (150 g.) and sodium chloride (30 g.) at 180° was added slowly with stirring, a mixture of homophthalic acid (18 g.) and quinol (11 g.). An orange-brown colour developed as the reaction proceeded and the temperature was not allowed to exceed 195°. The mixture was cooled and decomposed with water (1 l.) and concentrated hydrochloric acid (500 ml.), and the precipitate collected. The dried precipitate was extracted with boiling light petroleum (b. p. 100—120°), and the extract concentrated, filtered (charcoal), and allowed to crystallise. Recrystallisation from the same solvent yielded clusters of orange crystals, m. p. 179° (0·3 g., 1%) which when sublimed *in vacuo* were yellow (Found : C, 70·6; H, 3·95. $C_{15}H_{10}O_4$ requires C, 70·85; H, 3·95%). Light absorption : max. at 220, 242, 270, and 432 mμ (log ε 4·60, 4·43, 4·20, and 4·25 respectively) in *cyclo*hexane. When the filtrate from the above reaction was extracted with chloroform, and the latter treated with aqueous sodium hydrogen carbonate, acidification of the aqueous extract afforded o-(2 : 5-*dihydroxybenzoyl*)*phenylacetic acid* (I). Recrystallisation from water gave yellow crystals of the *hemihydrate*, m. p. 119° (Found : C, 64·4; H, 4·65. $C_{15}H_{12}O_5,\frac{1}{2}H_2O$ requires C, 64·1; H, 4·6%). Heating the acid *in vacuo* above its m. p. gave bright yellow needles of the anhydrous acid, m. p. 156° (Found : C, 66·35; H, 4·6. $C_{15}H_{12}O_5$ requires C, 66·1; H, 4·4%). The acid was converted into the dione (II) by the above procedure. It had m. p. and mixed m. p. 178°. 2 : 5-Dihydroxydeoxybenzoin-2′-carboxylic acid (IV) was also converted into the dione (II) by the same treatment. It had m. p. and mixed m. p. 179° (10%). The *diacetate* separated from benzene–light petroleum (b. p. 80—90°) in pale yellow crystals, m. p. 174° (Found : C, 67·7; H, 4·15. $C_{19}H_{14}O_6$ requires C, 67·45; H, 4·15%). Light absorption : max. at 252 and 290 mμ (log ε 4·43 and 4·01 respectively) in MeOH. It gave no ferric chloride colour. Reaction of the dione (II) with phenylhydrazine afforded a *product* as orange plates, m. p. 204° (from aqueous alcohol) (Found : C, 74·35; H, 5·75; N, 7·6. $C_{33}H_{26}O_5N_2$ requires C, 74·2; H, 5·4; N, 7·5%). Refluxing the dione (II) in methyl sulphate–acetone–potassium carbonate for 24 hr. gave the *trimethyl ether* as deep yellow crystals, m. p. 188° [from light petroleum (b. p. 100—120°)] (Found : C, 72·85; H, 5·45; OMe, 30·1. $C_{18}H_{16}O_4$ requires C, 72·95; H, 5·4; 3OMe, 31·4%). Light absorption : max. at 210, 255, and 310 mμ (log ε 4·35, 4·25 and 3·83 respectively) in MeOH.

Oxidation of the Trimethyl Ether.—The ether (0·15 g.) was dissolved in glacial acetic acid (5 ml.), and sodium dichromate (0·65 g.) in the same solvent (2·5 ml.) was added. After refluxing 30 min. the mixture was poured into water, a voluminous precipitate being formed. The *dilactone*, crystallised from benzene (charcoal), had m. p. 236° (Found : C, 65·2; H, 3·9. $C_{17}H_{12}O_6$ requires C, 65·4; H, 3·85%). Dissolution of 13·5 mg. of the dilactone in warm 0·025N-sodium hydroxide and back-titration with hydrochloric acid showed that 3·24 ml. of alkali were neutralised (required 3·44 ml.).

1′ : 4′-*Dimethoxy*-1 : 2-4 : 5-*dibenzo*cyclo*heptadiene*-3 : 7-*dione* (VI).—The above trimethyl ether (0·1 g.) was dissolved in glacial acetic acid (10 ml.) containing sulphuric acid (5 ml.; 2N). After 4 hr. on a steam-bath, the mixture was diluted with water and the precipitate collected. Crystallisation from light petroleum (b. p. 100—120°) gave yellow *dione*, m. p. 170° (40 mg.) (Found: C, 72·0; H, 4·9; OMe, 20·5. $C_{17}H_{14}O_4$ requires C, 72·3; H, 4·95; OMe, 22·0%). Light absorption: max. at 216, 255, and 320 mμ (log ε 4·38, 4·15, and 3·76 respectively) in MeOH. Remethylation with methyl sulphate gave the trimethyl ether, m. p. and mixed m. p. 188°. The 2 : 4-dinitrophenylhydrazone crystallised as the orange-yellow *dihydrate*, m. p. 240°, from aqueous alcohol (Found: C, 55·2; H, 4·5. $C_{23}H_{18}O_7N_4,2H_2O$ requires C, 55·4; H, 4·4%). The lemon-yellow 3 : 5-*dinitrobenzoate*, crystallised from benzene (charcoal), had m. p. 253° (Found: C, 60·3; H, 3·1. $C_{24}H_{16}O_9N_2$ requires C, 60·5; H, 3·35%).

3-(2 : 5-*Dihydroxyphenyl*)iso*coumarin* (III).—A mixture of homophthalic anhydride (8 g.), quinol (6 g.), and anhydrous stannic chloride (25 g.) was heated with stirring at 120° for 1 hr. After cooling, the rust-brown paste was warmed with dilute hydrochloric acid (1 : 1) for a short time, then cooled, and the precipited iso*coumarin* was collected and crystallised from aqueous acetic acid (charcoal), forming lustrous brown needles, m. p. 256° (2 g., 15%) which dissolved in hot aqueous sodium carbonate and gave an orange-brown precipitate with ferric chloride (Found: C, 70·55; H, 4·25. $C_{15}H_{10}O_4$ requires C, 70·85; H, 3·95%).

2 : 5-*Dihydroxydeoxybenzoin*-2′-*carboxylic Acid* (IV).—The above *iso*coumarin was warmed for 5 min. in aqueous 10% sodium hydroxide, cooled, and acidified. The precipitated *acid* crystallised from aqueous methanol (charcoal) in cream needles, m. p. 193° (90%) (Found: C, 66·0; H, 4·4. $C_{15}H_{12}O_5$ requires C, 66·1; H, 4·4%). The acid gave a green ferric colour and was reconverted into the *iso*coumarin in 10 min. at 250° or on treatment with cold anhydrous hydrogen fluoride.

3-(2 : 5-*Dimethoxyphenyl*)iso*coumarin*.—This was obtained from homophthalic anhydride and quinol dimethyl ether as for (III). The crude oil obtained was washed in ether with aqueous sodium carbonate, and with water, and evaporated. The remaining oil then solidified when dried *in vacuo*. Several crystallisations from aqueous methanol (charcoal) afforded pale yellow needles, m. p. 112° (Found: C, 72·4; H, 5·2. $C_{17}H_{14}O_4$ requires C, 72·4; H, 5·0%).

(2 : 5-*Dimethoxybenzylidene*)*phthalide*.—2 : 5-Dimethoxyphenylacetic acid (17 g.), phthalic anhydride (13 g.), and anhydrous potassium acetate (1 g.) were heated together at 240° for 2 hr. When cold, the solid residue was extracted with boiling glacial acetic acid (charcoal). The *phthalide* separated on cooling and recrystallised from ethanol in bright yellow needles, m. p. 159° (12 g., 49%) (Found: C, 72·15; H, 4·95. $C_{17}H_{14}O_4$ requires C, 72·35; H, 4·95%).

2′ : 5′-*Dimethoxydeoxybenzoin*-2-*carboxylic Acid* (XV).—The above phthalide (5 g.) was heated with potassium hydroxide (2 g.) in water (15 ml.) until dissolution was complete. Acidification of the ice-cold solution gave a sticky precipitate which was taken into ether. Evaporation of the solvent left a gum which solidified *in vacuo*. After being washed with a little ethyl acetate and then benzene, it crystallised from light petroleum (b. p. 50—60°) in clusters, m. p. 90° (2·5 g., 46%) (Found: C, 67·8; H, 5·1. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·35%). Heating this *acid* above its m. p. regenerated the phthalide.

(2 : 5-*Dihydroxybenzylidene*)*phthalide*.—(*a*) (2 : 5-Dimethoxybenzylidene)phthalide (0·5 g.) was refluxed for 3 hr. with hydriodic acid (5 ml.; *d* 1·7) in glacial acetic acid (2 ml.). Dilution with water then gave a precipitate which crystallised from aqueous alcohol (charcoal) in pale yellow plates, m. p. 224° (Found: C, 71·0; H, 3·95. $C_{15}H_{10}O_4$ requires C, 70·85; H, 3·95%). (*b*) By the same procedure 2′ : 5′-dimethoxydeoxybenzoin-2-carboxylic acid also gave the phthalide, m. p. and mixed m. p. 224°.

We are indebted to Mr. M. St. C. Flett and Dr. T. S. Robinson for infrared data.

THE UNIVERSITY, OLD ABERDEEN. [*Received, February 24th*, 1955.]

The Vapour Pressures of Nitric Acid Solutions. Part I. New Azeotropes in the Water–Dinitrogen Pentoxide System.

By L. Lloyd and P. A. H. Wyatt.

[Reprint Order No. 6177.]

Vapour pressures of the water–dinitrogen pentoxide system in the range 62—90% of N_2O_5 were measured directly at −10°, 0°, +10°, and +20° by a new static technique which involves the use of chlorofluorocarbon and Silicone oils as manometric fluids. Both the total vapour pressures and the vapour-phase compositions indicate the presence of two new azeotropes, one (with a maximum pressure) near the composition of pure nitric acid and the other (with a minimum pressure) at 87—88% of N_2O_5. An inconsistency in the former pressure and vapour-composition data in this region is thus removed. The minimum vapour pressure in the nitric acid–dinitrogen pentoxide system is attributed to the extensive ionization of dinitrogen pentoxide in dilute solution.

Wyatt (*Trans. Faraday Soc.*, 1954, **50**, 352) showed that the combined vapour pressure results obtained by Wilson and Miles (*ibid.*, 1940, **36**, 356) for the water–nitric acid system and by Berl and Saenger (*Monatsh.*, 1929, **54**, 1042) for the nitric acid–dinitrogen pentoxide system were not consistent with the finding that the vapour over 100% nitric acid had the same composition as the liquid, since the total pressure was represented as increasing through the composition: 100% of HNO_3. Vandoni's more recent results (*Mém. Services chim. État*, 1950, **35**, 63) and those of Vandoni and Laudy (*J. Chim. phys.*, 1952, **49**, 99) show a greater flattening of the pressure curve in this region, but are not extensive enough to provide a satisfactory solution.

We now believe this problem to have been solved by the discovery of two new azeotropes in the H_2O–N_2O_5 system. In addition to the well-known minimum vapour pressure at about 60% by weight of dinitrogen pentoxide (*i.e.*, 70% nitric acid), there is a maximun pressure near 85·7% of dinitrogen pentoxide (100% nitric acid), followed by a further minimum near 87·5% of dinitrogen pentoxide (" 102% " nitric acid). The pressure changes in this region are small, but are definitely established by a rapid and direct technique which has been developed for the accurate measurement of nitric acid vapour pressures. The novelty of this static method lies in the use of chlorofluorocarbon and Silicone oils as manometric fluids of low density in place of the more usual Bourdon gauge and mercury manometer.

Experimental

The apparatus is shown in Fig. 1. There was no disadvantage in having ground-glass joints and taps in the system when these were freshly greased with chlorofluorocarbon grease (Imperial Chemical Industries Limited "Fluorube" W). A magnetic stirrer operated by a solenoid actuated twice a second ensured the attainment of equilibrium and facilitated the removal of dissolved air from the liquid in the cell before taking measurements, and gave constant and reproducible stirring conditions. The Pyrex tubing in the vacuum line was of 9-mm. bore and that of the manometer limbs of 6 mm., and the length of tubing between T_1 and T_3 was kept as short as practicable to reduce the volume of exposed vapour. For evacuation a mercury diffusion pump was backed by a Cenco Hyvac oil-pump and protected by a liquid-air trap. In order to compare the suitability of two manometric fluids simultaneously a second manometer (omitted from the diagram) identical with that shown and fitted with separate taps was connected at $M'M'$. The manometers were housed in a wooden box with a glass front to protect their fluids, which have appreciable temperature coefficients of density, from fluctuations in temperature. This was normally 21—23° and was checked so that the appropriate oil density could be used. Differences of less than 10 cm. in the manometer levels were read with a cathetometer to 0·001 cm., but for larger differences glass and wooden scales were mounted behind the manometers and checked in sections against the cathetometer.

Experiments were carried out as follows. Approximately 100% nitric acid was prepared

(Wilson and Miles, *loc. cit.*; Hughes, Ingold, and Reed, *J.*, 1950, 2438; Dunning and Nutt, *Trans. Faraday Soc.*, 1951, **47**, 15) by distillation from a 1·3 : 1 (by volume) mixture of 98%-sulphuric and 70% nitric acids and stored in liquid air or deep freeze till required. For compositions below 100% of HNO_3, this acid was cooled and mixed with water. For compositions above 100% of HNO_3, dinitrogen pentoxide was prepared and mixed with the nitric acid (Dunning and Nutt, *loc. cit.*; see also Berl and Saenger, *loc. cit.*, and Gillespie, Hughes, and Ingold, *J.*, 1950, 2552). About 50 c.c. of the mixture were transferred to the weighed cell *C*, a sample was withdrawn for analysis, and the cell (having glass caps at the joints *X* and *Y*) was reweighed and then joined to the vacuum apparatus at *Y*, with the side-arm connected at *X* and carrying a bulb *S* as shown in Fig. 1. The cell *C* was then immersed in solid carbon dioxide–acetone until the contents were solid, T_1 was opened to the vacuum and the apparatus pumped out for several min. through T_1, T_2, T_3, and T_4. After *C* was isolated by closing T_1, the liquid was allowed to warm to about 5° and stirred to expel air. It was then frozen and pumped out as

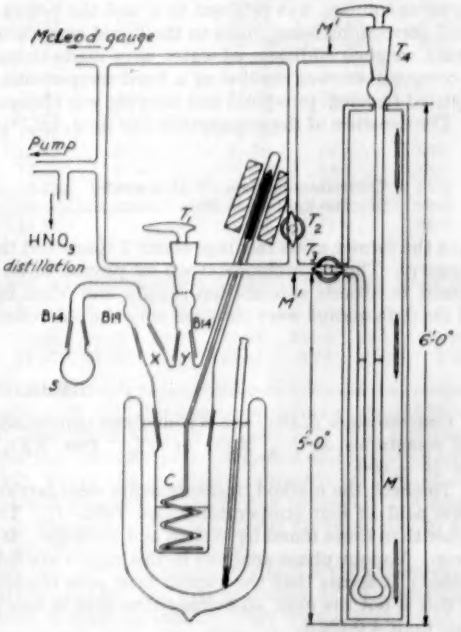


FIG. 1. *Apparatus for the determination of vapour pressures (manometer not to scale).*

before. This procedure was repeated until no further bubbles appeared on warming, after which T_2 was closed and *C* was connected with the manometer *M via* T_1 and T_3, T_4 still being open to the vacuum line.

The most reproducible manometer readings were obtained by warming the cell to about a degree above the temperature required and then bringing the bath (a Dewar flask fitted with a stirrer and thermometer) rapidly to the required temperature. The difference between the manometer limbs became constant and remained so after 10—15 min. from the time when the cell was first warmed, and T_1 was normally kept closed and T_2 open during this period to minimize errors due to the slight solubility of the acid vapours in the manometer fluids. A period of exposure of about 5 min., which usually sufficed for the measurements, was found to be well within the safety limit for absorption, and the manometer limbs were always pumped out thoroughly immediately after exposure. For measurements at 20° on the dinitrogen pentoxide side of the last azeotrope the pressures always steadily increased after the preliminary drop when the temperature was lowered from 21°. Decomposition of dinitrogen pentoxide in the vapour was obviously becoming important here and the (less accurate) vapour pressures quoted in Table 2 were in this case estimated by extrapolation.

When taking samples for estimating vapour-phase compositions, the (weighed) bulb *S* was

cooled in solid carbon dioxide–acetone to collect about 1 c.c. of distillate (usually about 20 min.). Taps T_2 and T_4 were then closed, the contents of C frozen, T_1 was connected to the vacuum line, and air was allowed to leak into C *via* the liquid-air trap. S was then disconnected, its joint rapidly wiped free from grease and immediately closed with a B14 cap. When it had reached the laboratory temperature, the bulb was dried and weighed. The contents were then re-frozen, the stopper removed, and bulb and stopper dropped into a 500 c.c. wide-mouthed, stoppered bottle containing 100 c.c. of distilled water. The acid sample thus diluted was titrated directly (phenolphthalein) with 0·5N- and 0·05N-NaOH which was standardized against sulphuric acid made up from the cryoscopically determined 100% acid (Kunzler and Giauque, *J. Amer. Chem. Soc.*, 1952, **74**, 3472) and checked with potassium hydrogen phthalate and succinic and adipic acids. Precautions were taken to exclude carbon dioxide. The weights of nitric acid samples were generally such that 50 ml. of the 0·5N-alkali (by pipette) left a small excess of acid to be titrated by the 0·05N-alkali.

Several experiments were usually carried out on each solution in the cell C. In some runs the same solution was retained in C and the pressure was measured at different temperatures, small corrections being made to the liquid composition if vapour samples were withdrawn. In others, weighed additions of water were made through X (after freezing the acid) and a series of compositions was studied at a fixed temperature. Whenever air was allowed into the cell, repeated freezing, pumping, and thawing was always carried out subsequently.

The densities of the manometric oils (in g. cm.$^{-3}$) were found with a pyknometer to be

	0°	10°	20°
Chlorofluorocarbon oil (thin grade)	1·9723	1·9606	1·9479
Silicone fluid (M.S. 200)	0·9859	0·9775	0·9685

Thus the former gives readings about 7 times and the latter about 14 times as great as those of mercury. The chlorofluorocarbon oil proved to be excellent for the purpose, but the Silicone seemed to absorb vapours too readily and often became cloudy after only a short exposure. All the data quoted were obtained with the chlorofluorocarbon manometer.

Results

Concentration Scales.—It is sometimes convenient to refer to a given solution as a% HNO_3, and sometimes as b% N_2O_5 or c% "free N_2O_5." The relationships are: $b = 0{\cdot}8570a$, $c = 7b - 600$.

To check the method, measurements were carried out on acids of composition 72—100% of nitric acid at four temperatures (see Table 1). The total pressures at 20° are about 2 mm. higher than those found by Wilson and Miles (*loc. cit.*) except at 99·8% where our value is 1 mm. lower. Vapour-phase analyses in this region are being further investigated and have not been quoted; it seems that the vapour over pure nitric acid contains about 0·2% excess of water. (If this is not the case, all composition data in this paper will be subject to a correction of not more than +0·2%.)

Table 1. *Vapour pressures of nitric acid solutions.*

Concn.	Total vapour pressures (mm. Hg)				Concn.	Total vapour pressures (mm. Hg)			
(% HNO_3)	−10°	0°	10°	20°	(% HNO_3)	−10°	0°	10°	20°
72·4	1·10	2·02	3·69	6·46	91·8	4·83	9·82	18·06	32·09
77·7	1·31	2·77	5·52	10·45	96·3	6·30	12·64	23·35	41·47
83·3	2·26	4·67	8·89	16·41	99·8	6·97	14·02	26·42	46·96
87·1	3·40	6·56	12·54	22·09					

Table 2 contains the results for compositions above 100%: relative liquid compositions are known to two places of decimals. At the highest concentrations the withdrawal of vapour samples affected the liquid composition appreciably and the figures in parentheses represent interpolated mean values of liquid concentration and vapour pressure calculated from the values before and after sampling the vapour. At all temperatures unmistakable signs of azeotropic behaviour are shown both in the total pressures and in the vapour-phase compositions (see Fig. 2). Corroborative evidence is also provided by the behaviour of the vapour at 20°: when progressive amounts of water were added to a concentrated solution of dinitrogen pentoxide at that temperature the manometer readings increased with time until the minimum pressure was reached,

after which point the normal constant readings were obtained. This change occurred quite sharply, as would be expected from a rapid change in the partial pressure of dinitrogen pentoxide in this region. In order to define more accurately the shape of the curve in the neighbourhood

TABLE 2. *Vapour pressures of* N_2O_5 *solutions at* $-10°$, $0°$, $10°$, *and* $20°$.

N_2O_5 in liquid (%)	p (mm. Hg)	N_2O_5 in vapour (%)	N_2O_5 in liquid (%)	p (mm. Hg)	N_2O_5 in vapour (%)	N_2O_5 in liquid (%)	p (mm. Hg)	N_2O_5 in vapour (%)
Temp. −10°			Temp. 0°			Temp. 0°		
89·08	11·71	—	89·17	25·61	—	86·57	13·58	—
88·75	9·17	—	(89·12)	(24·43)	96·3	86·00	13·87	85·5
(88·71)	(8·80)	93·7	89·08	23·25	—	85·72	13·99	85·5
88·05	6·76	89·6	(88·99)	(21·3)	95·0			
87·63	6·30	87·5	88·91	19·47	—	Temp. 10°		
87·63	6·29	87·2	(88·89)	(19·30)	94·2	88·02	30·13	91·2
86·97	6·44	86·0	88·66	16·71	—	87·84	25·84	88·0
86·50	6·71	85·5	(88·58)	(16·2)	92·0	87·39	25·87	87·6
85·81	6·90	—	88·64	17·1	—	86·86	25·40	86·9
			(88·58)	(16·2)	91·6	86·51	25·65	—
Temp. 0°			88·14	14·64	90·6	86·50	25·66	86·3
89·68	37·83	—	88·10	14·05	89·8	85·70	26·26	85·4
(89·63)	(36·66)	97·6	87·85	13·16	87·6			
89·59	35·65	—	87·83	13·16	—	Temp. 20°		
89·58	35·49	—	87·75	13·13	87·6	87·76	52·5	92·4
(89·52)	(33·44)	97·1	87·61	12·98	87·4	87·40	48·1	88·2
89·47	31·39	—	87·38	13·18	85·5	87·15	46·6	87·3
(89·26)	(26·4)	95·9	87·31	13·16	85·8	86·91	46·8	86·6
89·26	26·26	—	87·10	13·36	—	86·63	47·0	86·2
(89·24)	(25·9)	96·0						

of 100% HNO_3 the following results obtained by adding small amounts of water to 99·6% nitric acid at 0° have also been plotted in Fig. 2.

HNO_3 (%)	99·60	99·33	98·97	98·63	98·29	97·63	94·91	92·93	90·53	87·11	84·99
p (mm. Hg)	13·96	13·92	13·80	13·74	13·57	13·26	12·01	10·51	8·78	6·56	5·40

Increase of temperature appears to shift the minimum vapour pressure towards the composition of pure nitric acid: from graphs it is estimated that this azeotrope occurs at about 88% of dinitrogen pentoxide at −10°, 87·8% at 0°, and about 87% at 10° and 20°. The minimum pressure is always of the order of 1 mm. below the value for pure nitric acid and the azeotropic behaviour is therefore most marked at −10°, where the depression amounts to 10% of the vapour pressure of pure nitric acid. The partial pressures of dinitrogen pentoxide and nitric acid do not satisfy the simple Duhem–Margules equation well, but this is probably due to the great precision in analysis required for such a sensitive test in this region.

The total-pressure data of Berl and Saenger (*loc. cit.*) are considerably higher than the present values, presumably owing to vapour phase decomposition, and give no indication of azeotropes. Those of Vandoni (at 0°, *loc. cit.*) are, however, in good agreement apart from a slight shift in the composition axis, but show only one point in the azeotropic region (at 86·4% of dinitrogen pentoxide), for which, however, the static pressure is clearly too high (Fig. 2). Vandoni appears to have overlooked the evidence from his dynamic results at this point, which give not only a lower total pressure than at 100% of nitric acid but a reduced concentration of dinitrogen pentoxide in the vapour (3% of free dinitrogen pentoxide) as compared with the liquid (5% of free dinitrogen pentoxide).

The Effect of Dinitrogen Tetroxide on the Azeotropes.—All solutions of concentration greater than 85·7% of dinitrogen pentoxide were more or less pale yellow in colour and it was therefore necessary to investigate the effect of dinitrogen tetroxide on the appearance of the azeotropes. Liquid dinitrogen tetroxide was prepared from lead nitrate (Addison and Thompson, *J.*, **1949**,

TABLE 3. *Effect of adding* N_2O_4 to 85·5% N_2O_5 *at* 0°.

g. N_2O_4/100 g. acid	0·000	0·573	1·266	2·468	7·125
p, mm. Hg	14·02	14·76	15·21	15·86	18·46

TABLE 4. *Effect of adding* N_2O_4 *to* 88·1% N_2O_5 *at* 0°.

g. N_2O_4/100 g. acid	0·000	0·711	2·182	4·147	7·387
p, mm. Hg	14·66	15·93	17·93	20·47	24·75

S218) and dissolved in pure nitric acid to make a concentrated solution, which could then be manipulated in a weight pipette. Successive additions were made to acids of 85·5% and 88·1% of dinitrogen pentoxide and the total pressures at 0° were noted (Tables 3 and 4). The dinitrogen tetroxide clearly increased the total pressure to a greater extent in the dinitrogen pentoxide-rich solution (*i.e.*, 88·1%, near the composition of minimum vapour pressure) than in the purer nitric acid, whence it was concluded that the effect of the dinitrogen tetroxide impurity would be to mask rather than enhance the appearance of azeotropes. The colour of a 0·5% solution of dinitrogen tetroxide was also considerably deeper than those encountered during the work, so that it could be estimated that the tetroxide impurity when present was only of the order 0·1%.

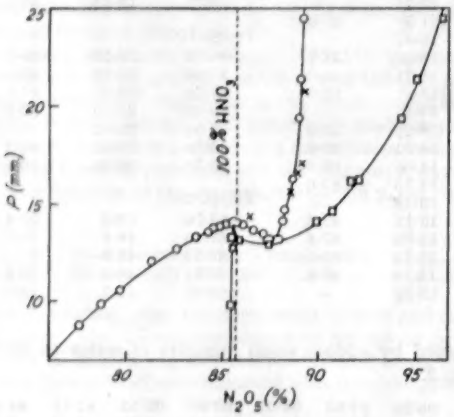


FIG. 2. *Vapour pressures in the neighbourhood of* 100% HNO_3 *at* 0°.
○ *Liquid composition.*
□ *Vapour composition.*
× *Vandoni's static data.*

DISCUSSION

Vapour pressures in the nitric acid–dinitrogen pentoxide system now emerge with a similar pattern to those in the water–nitric acid system. It therefore seems likely that the same explanation will hold for both systems, *i.e.*, the minimum in the vapour pressure curve is mainly due to the extensive ionization of one constituent in dilute solution (dinitrogen pentoxide in nitric acid and nitric acid in water), which produces a relative lowering of the partial pressure of that constituent as compared with its contribution to the pressure of more concentrated solutions. An increase in the self-dissociation of nitric acid in the liquid phase would reduce the initial depression of p_{HNO_3} caused by added N_2O_5 and would therefore tend to mask the effect just described. Thus the reduction in the importance of the dinitrogen pentoxide–nitric acid azeotrope with increasing temperature could be due to an accompanying increase in the self-dissociation of nitric acid.

Complications due to the simple dissociation $2HNO_3 \rightleftharpoons H_2O + N_2O_5$ in the vapour seem most unlikely in view of the following argument. The vapour-phase reaction $4HNO_3 \rightleftharpoons 2H_2O + 4NO_2 + O_2$ has a measurable equilibrium at the pressures involved in these experiments; whence for $4HNO_3 \rightleftharpoons 2H_2O + 2N_2O_5$ to be measurable the equilibrium $2N_2O_5 \longrightarrow 4NO_2 + O_2$ would also have to be measurable. But this would be in conflict with kinetic work, in which the decomposition of dinitrogen pentoxide is described as going to completion (Daniels and Johnstone, *J. Amer. Chem. Soc.*, 1921, **43**, 53). Thus the equilibrium vapour concentration of dinitrogen pentoxide in the presence of free water must be very small. It also follows that if either water or dinitrogen pentoxide is volatile as such over pure nitric acid (dissociated in the liquid) the other must be effectively involatile.

SHEFFIELD UNIVERSITY. [*Received, February 25th*, 1955.]

Alkaloids of Australian Strychnos *Species. Part II.* The Constitution of Strychnospermine and Spermostrychnine.*

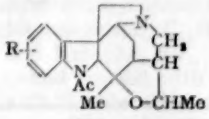
By F. A. L. Anet and Sir Robert Robinson.

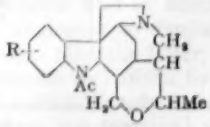
[Reprint Order No. 6190.]

The structures of the two alkaloids of *Strychnos psilosperma*, strychnospermine and spermostrychnine, have been determined. The former alkaloid is a methoxy-derivative of the latter, which has been related to strychnine by way of deoxydihydrospermostrychnine. The position of the methoxyl group of strychnospermine has been determined by ultraviolet spectroscopy and by colour reactions, including the formation of a rhodamine by demethylation and condensation with phthalic anhydride.

Strychnospermine, the main alkaloid of the Australian plant, *Strychnos psilosperma*, was assigned the formula $C_{21}H_{28}O_3N_2$ by Anet, Hughes, and Ritchie (*Nature*, 1950, **166**, 476), later changed to $C_{22}H_{28}O_3N_2$ (*idem*, *Austral. J. Chem.*, 1953, **6**, 58). It was found (*loc. cit.*, 1953) to contain one methoxyl and at least two *C*-methyl, but no *N*-methyl groups in the molecule. The alkaloid was a tertiary base, forming a hydrochloride and a methiodide, and contained a *N*-acetyl group as shown by hydrolysis with acid or alkali to deacetylstrychnospermine, $C_{20}H_{26}O_2N_2$, which gave a basic *N*-nitroso-derivative. The colour reactions of the alkaloid were similar to those of strychnine (positive Otto reaction) whilst those of the deacetyl base resembled those of strychnidine or strychnic acid. The remaining oxygen atom appeared to be unreactive and was assumed to occur in a cyclic ether group. On the basis of these reactions, the ascertained molecular structure of strychnine, and Woodward's theory of the biogenesis of that alkaloid (*Nature*, 1948, **162**, 155), the most probable formula for the base was considered to be (I; R = OMe). Another alkaloid, spermostrychnine, $C_{21}H_{26}O_2N_2$, was found in smaller amount in the same plant (*loc. cit.*, 1950). It resembled strychnospermine, but it did not contain a methoxyl group and

(I)





(II)

was therefore considered to be (I; R = H) (*loc. cit.*). Several other structures, including (II), were considered for these bases, but were thought to be less likely.

In the present work strychnospermine was first investigated because of its greater accessibility. The question of the number of *C*-methyl groups in strychnospermine has been re-examined, as it was of importance in connexion with the substituents in the oxide ring and because the figures previously obtained by Anet *et al.* (*loc. cit.*) were not entirely conclusive. It became evident from new determinations that deacetylstrychnospermine contained only one *C*-methyl group and strychnospermine two such groups. A macro-determination with the former base gave only 85% of the amount of acetic acid corresponding to one *C*-methyl group. The microanalytical values tended to be higher for some unknown reason. Similar high values have been found by Elderfield and Gray for certain alstonine derivatives (*J. Org. Chem.*, 1951, **16**, 521), and by Karrer, Eugster, and Rüttner for emetine (*Helv. Chim. Acta*, 1948, **31**, 1219), as well as by the present authors in the case of ajmaline and some of its derivatives [Anet, (Mrs. D. Chakravarti), Robinson, and Schlittler, *J.*, 1954, 1242]. Of the two formulæ (I and II) already mentioned, (II) should be preferred to (I) on these, and also on biogenetic grounds.

The ultraviolet absorptions of strychnospermine and of deacetylstrychnospermine are shown in Fig. 1. These are consistent with a *N*-acetyldihydroindole and a dihydroindole structure respectively, containing a methoxyl group in the benzene ring (Raymond Hamet,

* Part I, *Austral. J. Chem.*, 1953, **6**, 58.

Ann. pharm. franç., 1950, **8**, 482). The infrared spectrum of strychnospermine showed an intense band at 6·06 μ and no absorption indicative of a NH or OH group. The deacetyl base, on the other hand, showed no carbonyl absorption, but had a band at 3·00 μ, which could be due to a NH group. The absence of a strong band in both these compounds at about 13·4 μ indicated the absence of a 1 : 2-disubstituted benzene ring, thus proving that the methoxyl group was attached to the benzene ring, but it was not possible to assign the exact position of this substituent from the infrared spectra alone.

With boiling hydrobromic acid strychnospermine smoothly gave deacetyldemethylstrychnospermine dihydrobromide by hydrolysis of both the acetyl and the methoxyl group. This salt was very soluble in water, but was readily hydrolysed to the sparingly soluble monohydrobromide in water, a reaction which took place immediately on addition of sodium acetate to the solution of the dihydrobromide in dilute acid. The second basic

FIG. 1.

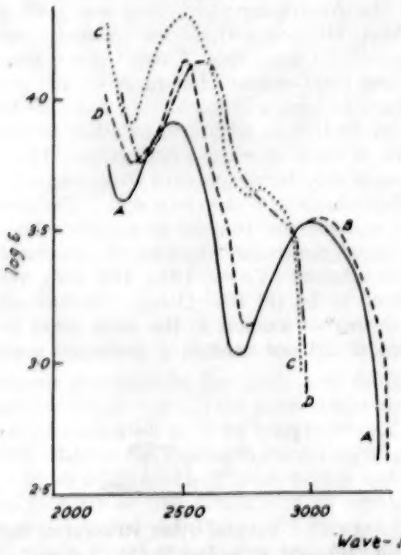
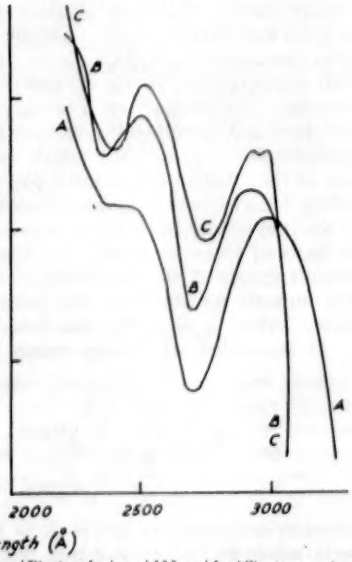


FIG. 2.



Wave-length (Å)

FIG. 1. *Absorption spectra of* (*A*) *deacetylspermostrychnine*, (*B*) *strychnic acid* N-*oxide*, (*C*) *spermostrychnine, and* (*D*) *strychnine.*

FIG. 2. *Absorption spectra of* (*A*) *deacetylstrychnospermine*, (*B*) *strychnospermine, and* (*C*) α-*colubrine.*

function is therefore a weak one, and is in fact analogous to N(*a*) in strychnidine (Clemo, Perkin, and Robinson, *J.*, 1927, 1589). Although the free base was not obtained crystalline it was observed to be easily soluble in dilute aqueous sodium hydroxide to give a solution which was oxidised rapidly in the air. Reaction of the dihydrobromide with acetic anhydride in the presence of anhydrous sodium acetate at 100° readily gave demethylstrychnospermine, which was soluble in alkali and was converted into strychnospermine methiodide by methyl iodide in alcoholic alkali. Fusion of deacetyldemethylstrychnospermine dihydrobromide with phthalic anhydride gave an intense rhodamine-like dye (similar to Rhodamine 6G in colour and fluorescence), showing that the phenolic hydroxyl group was *meta* to the nitrogen atom.

Reduction of strychnospermine with lithium aluminium hydride gave deacetyl-*N*-ethylstrychnospermine, which on demethylation with hydrobromic acid, followed by fusion with phthalic anhydride, afforded a rhodamine dye, the colour of which was bluer (similar to Rhodamine B) than that of the dye obtained from deacetyldemethylstrychnospermine. The colour of the former dye was identical with that of the rhodamine dye obtained from

demethylated hexahydro-7-methoxy-11 : *N*-dimethylcarbazole (prepared by Dr. M. F. Millson), but very different from that obtained from demethylated hexahydro-5-methoxy-11 : *N*-dimethylcarbazole, which gave a much bluer red, almost red-purple, dye with a bright red instead of yellow-green fluorescence.

The position of the methoxyl group in strychnospermine was confirmed by a comparison of the ultraviolet spectra of the alkaloid and of its deacetyl derivative with those of model compounds prepared by Dr. H. T. Openshaw. We are greatly indebted to Dr. Openshaw for communicating these results to us before their publication.

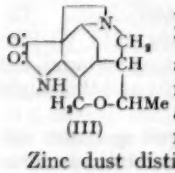
	Base		Acetyl deriv.	
	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε
Hexahydro-5-methoxycarbazole	(231)	8200	254	14,000
	287·5	1200	297	6,300
Hexahydro-6-methoxycarbazole	243	7500	262	15,500
	308·5	3400	296	4,200
Hexahydro-7-methoxycarbazole	(236)	4800	253·5	9,700
	296	4300	295·5	6,200
Hexahydro-8-methoxycarbazole	243	6900	256	11,900
	288	2100	288	2,900
Deacetylstrychnospermine	(242)	3900	251	9,100
	300	3600	293	4,600

The methoxyl group of strychnospermine is in the same relative position as that of β-colubrine, and indeed the spectra of the two alkaloids are very similar (Raymond Hamet, *loc. cit.*) (see Fig. 2).

Reduction of bromostrychnospermine with lithium aluminium hydride afforded bromodeacetyl-*N*-ethylstrychnospermine, which gave intense colour reactions with traces of oxidising agents.

Strychnospermine *N*-oxide was obtained in a hydrated form by the action of aqueous hydrogen peroxide on the base, but it could not be converted into an analogue of *pseudo*-strychnine with potassium chromate (Bailey and Robinson, *J.*, 1948, 703). Strychnospermine methiodide, like dihydrostrychnine methiodide, was unaffected by sodium amalgam; it gave deacetylstrychnospermine methiodide on hydrolysis with dilute acid.

Oxidation of demethylstrychnospermine with chromic acid in dilute sulphuric acid gave a water-soluble compound, $C_{15}H_{20}O_3N_2$ (III), analogous to dioxonucidine (Leuchs and Kröhnke, *Ber.*, 1930, **63**, 1045). Like the latter, the above compound reacted with hydrogen peroxide in barium hydroxide solution with the liberation of one mol. of carbon dioxide and the formation of an amino-acid, which, however, was not obtained crystalline. The infrared spectrum of this *apo*spermostrychine (III) showed bands at 5·55, 5·68, 5·78, and 6·00 μ in the carbonyl region, consistent with a five-membered ring keto-amide.



(III)

Zinc dust distillation of deacetylstrychnospermine afforded 3-ethylpyridine, isolated as the picrate, and a neutral fraction which gave a strong Ehrlich reaction.

Attempts were made to open the postulated ether ring in strychnospermine or in one of its derivatives, but it is known that, although simple derivatives of basic cyclic ethers are easily split by hydrobromic acid (cf. Cerkovnikov and Prelog, *Annalen*, 1938, **535**, 37), more complex compounds, such as the various dihydrostrychnidines, are extremely stable (Wieland and Jennen, *Annalen*, 1940, **545**, 99; Perkin and Robinson, *J.*, 1929, 964). It was therefore expected that vigorous conditions would be required in the present case, and indeed deacetyldemethylstrychnospermine was recovered unchanged after being heated with 65% hydrobromic acid, in a sealed tube, at temperatures up to 150°. At higher temperatures the product contained some non-ionic bromine, showing that the reaction had taken place to some extent, but the resulting aminophenol readily suffered oxidation and no pure substance could be isolated. This reaction was not further investigated as it was realised that spermostrychnine, which does not contain a methoxyl group, would be more amenable to the above line of attack.

The ultraviolet spectra of spermostrychnine and of its deacetyl derivative are shown in Fig. 2 and are almost identical with those of strychnine and of strychnic acid *N*-oxide

respectively (Prelog and Szpilfogel, *Helv. Chim. Acta*, 1945, **28**, 1671). The infrared spectra of the first two compounds showed features analogous to those of the corresponding strychnospermine series, except that in the first two a strong band was present at about 13·3 μ, characteristic of an *o*-disubstituted benzene ring.

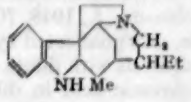
It was realised by Anet *et al.* (*loc. cit.*) that spermostrychnine would most likely prove to be demethoxystrychnospermine, and this has now been proved to be the case by oxidising spermostrychnine with chromic acid. The compound obtained, $C_{15}H_{20}O_3N_2$, was identical, as shown by m. p. and mixed m. p., as well as by comparison of rotations and infrared spectra, with the compound (III) obtained by the oxidation of demethylstrychnospermine.

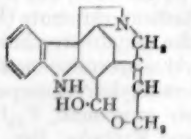
Zinc dust distillation of deacetylspermostrychnine hydrobromide gave a mixture of alkylindoles and, in the basic fraction, 3-ethylpyridine. Traces of carbazole or of an alkylcarbazole were probably also present, but the amount obtained was too small for purification. The formation of the above degradation products is obviously consistent with the structure proposed for the alkaloid.

The *N*-oxide of spermostrychnine reacted only slowly with aqueous potassium chromate solution, but it ultimately gave a base, which behaved like *pseudo*strychnine in giving a neutral nitroso-compound. This could not be crystallised and was not further investigated.

By the action of hydrogen bromide in acetic acid (50% w/v) on deacetylspermostrychnine at 180—200°, a product was obtained which contained much non-ionic bromine. It was not isolated in a pure condition but its solution in acetic–hydrobromic acid was directly reduced with zinc dust. The resultant base was acetylated and isolated as a crystalline perchlorate. The pure salt, $C_{21}H_{28}ON_2,HClO_4,1{\cdot}5H_2O$, lost a part of its water of crystallisation at 117° and all of it at 130°. The regenerated base, although not crystalline, gave satisfactory analyses for $C_{21}H_{28}ON_2$ after sublimation. This deoxydihydrospermostrychnine must have arisen by reductive removal of the cyclic ether oxygen atom of spermostrychnine and therefore should have the structure (IV). It can be seen that

(IV)



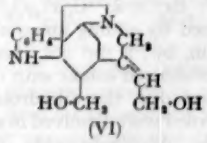


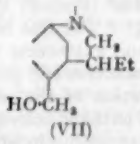
(V)

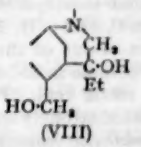
such a compound should be obtainable from strychnine by suitable degradation. The Wieland–Gumlich aldehyde (V) (Wieland and Gumlich, *Annalen*, 1932, **494**, 191; Wieland and Kazine, *ibid.*, **1933**, **506**, 60) appeared to be the most promising starting material, but it should be noted that several stereoisomers of the structure (IV) can exist and this might well have confused the issue.

Reduction of the Wieland–Gumlich aldehyde, which from its infrared spectrum was shown to exist in the cyclic form (V), with lithium aluminium hydride in tetrahydrofuran solution, or better with potassium borohydride in aqueous alcohol, gave the corresponding alcohol (VI). The reduction of this with hydrogen in the presence of palladium–charcoal in acetic acid proceeded readily, but it was found that if the hydrogenation was stopped after the absorption of one mol. of hydrogen much unchanged starting material could be recovered, and that it was not until nearly two mols. of hydrogen had been taken up that a seemingly homogeneous compound was obtained. The beautifully crystalline dihydrochloride of the reduced base was purified by several recrystallisations from aqueous acetone. This salt analysed for $C_{19}H_{26}O_2N_2,2HCl$, even when dried at 100° *in vacuo*, and it contained one *C*-methyl group. The infrared spectrum showed that it contained no acetone of crystallisation. The regenerated base, after several recrystallisations from aqueous methanol, followed by drying at room temperature, or at 100°, or by sublimation *in vacuo*, did not give reproducible analytical figures. The results were always intermediate between those required for $C_{19}H_{26}O_2N_2$ and for $C_{19}H_{26}ON_2$ (see Experimental section), and they also showed the presence of a *C*-methyl group. Although the analytical results were so unsatisfactory the compound appeared to be pure and showed a sharp and constant m. p. The reason for these peculiar results could not be ascertained. Since the substance contains

a *C*-methyl group it may be (VII), which has the latter formula and could be produced by the hydrogenolysis of the allylic hydroxyl group, or (VIII), which has the alternative formula and could arise by a preliminaty allylic rearrangement followed by hydrogenation of the vinyl group.

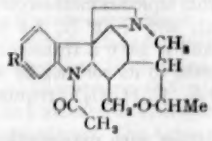

(VI)

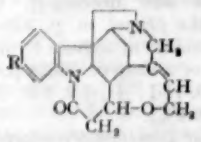

(VII)


(VIII)

Nevertheless, treatment of the hydrogenated compound with hydrogen bromide in acetic acid (50% w/v) at 180—200°, followed by reduction with zinc dust and acetic acid and acetylation, gave a base, isolated as the perchlorate, $C_{21}H_{28}ON_2,HClO_4,1{\cdot}5H_2O$.

(IX)




(X)

This had the same crystalline form, m. p. and mixed m. p., solubility, rotation, and infrared spectrum as had deoxydihydrospermostrychnine perchlorate. Thus the carbon skeleton of the alkaloids of *S. psilosperma* can be regarded as established and (IX; R = H or OMe) represents the most probable position of the oxide ring. It is seen that there is a remarkable correspondence between the structures of, on the one hand, strychnine (X; R = H) and spermostrychnine (IX; R = H), and, on the other hand, between β-colubrine (X; R = OMe) and strychnospermine (IX; R = OMe).

Experimental

Strychnospermine.—The alkaloid was recrystallised from aqueous methanol and formed colourless needles, m. p. 208—209° (Found: C, 71·6; H, 7·7; *C*-Me, 8·7, 8·5, 8·4. Calc. for $C_{22}H_{26}O_3N_2$: C, 71·7; H, 7·7; 2*C*-Me, 8·2%).

Deacetylstrychnospermine.—The *base*, when crystallised from aqueous methanol and then sublimed *in vacuo*, formed colourless prisms, m. p. 221—222°, $[\alpha]_D^{20}$ −117° (*c*, 2·43 in $CHCl_3$) (Found: *C*-Me, 5·6, 5·6, 5·5. $C_{20}H_{24}O_2N_2$ requires 1*C*-Me, 4·6%). A macrodetermination of *C*-methyl, using 1·96 g. of the base, by Huebner and Troxell's method (*J. Org. Chem.*, 1953, **18**, 736) gave 3·9%; this value may be slightly low as the distillation was stopped after the collection of 800 c.c. of aqueous solution.

Deacetylstrychnospermine Methiodide.—Strychnospermine methiodide (0·5 g.) was boiled with concentrated hydrochloric acid (10 c.c.) and water (10 c.c.) for 2 hr. After dilution to 50 c.c. with water, potassium iodide was added to precipitate the *methiodide* which crystallised from water in colourless needles, m. p. 301—303° (Found: C, 54·4; H, 6·5; N, 5·5. $C_{21}H_{29}O_2N_2I$ requires C, 53·9; H, 6·3; N, 6·0%).

Strychnospermine N-Oxide.—A mixture of strychnospermine (2 g.), hydrogen peroxide (2·5 c.c. of 30%), and water (200 c.c.) was heated on a steam-bath for 1 hr., and then boiled for 5 min. after the addition of a little platinum black. On cooling, the filtered solution deposited colourless, glistening, flat needles (1·7 g.), m. p. 261—263° (decomp.). The *N-oxide* recrystallised from water, in which it was only sparingly soluble in the cold (Found: C, 60·4; H, 8·0. $C_{22}H_{28}O_4N_2,3H_2O$ requires C, 60·3; H, 7·8%). Strychnospermine *N*-oxide (1 g.) was dissolved in boiling water (100 c.c.) containing potassium chromate (0·1 g.). The mixture was refluxed for 8 hr., but even after this time only a small amount of a deep red precipitate had separated, and it did not give the reactions of a carbinol-amine. The solution smelled of formaldehyde, which was isolated in small amount as its dimedone derivative.

Deacetyldemethylstrychnospermine.—A mixture of strychnospermine (18 g.) and 40% hydrobromic acid (100 c.c.) was heated under reflux for 1½ hr. Water (300 c.c.) was added and the

solution cooled to 0°, and, after several hours, filtered through sintered glass. The pink crystals (22 g.) of the *dihydrobromide* were washed with alcohol, then with ether, and crystallised from dilute hydrobromic acid in large prisms, m. p. 365° (decomp.) (Found: C, 45·2; H, 6·2; Br, 31·5. $C_{19}H_{24}O_3N_2,2HBr,2H_2O$ requires C, 44·7; H, 5·9; Br, 31·3%). Addition of sodium acetate to a solution of the salt in dilute acid caused the separation of the sparingly soluble crystalline *monohydrobromide*, m. p. 340° (Found: C, 58·5; H, 6·5; Br, 20·8. $C_{19}H_{24}O_3N_2,HBr$ requires C, 58·1; H, 6·4; Br, 20·3%). The free base was obtained by adding ammonia to a solution of one of the above salts and extracting with chloroform, but it did not crystallise. It was soluble in sodium hydroxide solution and gave a deep brownish-red colour with concentrated nitric acid. For the preparation of the related rhodamine dye, the dihydrobromide was heated strongly with an excess of phthalic anhydride and the cooled melt dissolved in alcohol.

Demethylstrychnospermine.—Deacetyldemethylstrychnospermine dihydrobromide (10 g.) was heated with acetic anhydride (60 c.c.) and anhydrous sodium acetate (3·3 g.) for an hour on a steam-bath. Water (140 c.c.) was added to destroy the excess of acetic anhydride, and the solution, after cooling in ice, was made alkaline with ammonia. The colourless precipitate was collected, a little more being obtained by chloroform extraction of the solution [total yield, 7·1 g.; m. p. 313—320° (decomp.)]. Crystallisation from aqueous methoxyethanol gave glistening needles of the *phenol*, m. p. 325—327° (decomp.), $[\alpha]_D^{22}$ +82° (*c*, 2·4 in 0·1N-HCl). The substance was soluble in sodium hydroxide solution and it gave a transient blue-violet colour on the addition of a drop of dilute potassium dichromate to its solution in 80% sulphuric acid (Found: C, 70·9, 71·1; H, 7·2, 7·5; N, 8·3; *C*-Me, 9·5. $C_{21}H_{26}O_3N_2$ requires C, 71·2; H, 7·4; N, 7·9; 2*C*-Me, 8·4%).

Methylation of Demethylstrychnospermine.—Methylation with diazomethane in chloroform–methanol was not very satisfactory, owing to the low solubility of the compound, and no strychnospermine could be isolated. By heating demethylstrychnospermine with excess of methyl iodide in methanol containing one mol. of sodium methoxide, a good yield of strychnospermine was obtained, having m. p. and mixed m. p. 335—337° (decomp.).

Deacetyl-N-ethylstrychnospermine.—A solution of strychnospermine (0·2 g.) in chloroform (10 c.c.) was added to one of lithium aluminium hydride (0·1 g.) in ether (50 c.c.), and the mixture heated under reflux for 1½ hr. Excess of the reagent was decomposed with ethyl acetate, and then sodium hydroxide solution (20 c.c. of 5%) added. The ethereal layer was separated and on evaporation left a colourless oil which crystallised from light petroleum in rectangular and hexagonal prisms (0·15 g.), m. p. 130—131°. Recrystallisation afforded the *base* as clusters of prisms, m. p. 131—131·5° (Found: C, 74·6; H, 8·4, 8·6; N, 8·1, 8·1. $C_{22}H_{30}O_2N_2$ requires C, 74·6; H, 8·6; N, 7·9%). The new base was readily soluble in organic solvents and gave an intense crimson-red colour with ferric chloride in weak acid solution, and a crimson colour with concentrated nitric acid. It coupled readily with diazobenzenesulphonic acid to give an indicator-type dye. The compound was demethylated by boiling it for 1 hr. with 50% hydrobromic acid. The salt obtained from this reaction was fused with phthalic anhydride as described above. The colour of the resulting dye was identical with that of the dye obtained by demethylating hexahydro-7-methoxy-11 : *N*-dimethylcarbazole and fusing the product with phthalic anhydride. Both dyes closely resembled Rhodamine B in respect of colour, tinctorial intensity, and fluorescence.

Deacetylbromo-N-ethylstrychnospermine.—Bromostrychnospermine (0·5 g.), suspended in dry ether (40 c.c.), was added to a solution of lithium aluminium hydride (0·2 g.) in ether (40 c.c.). After boiling under reflux for 2 hr., the mixture was worked up as described above, to give a colourless oily base, which was converted into the *picrate* in alcohol. The salt, after several recrystallisations from aqueous alcohol, was obtained as yellow needles, m. p. *ca.* 210° with sintering at 195° (Found: C, 51·2; H, 4·8; N, 10·7; Br, 12·5. $C_{28}H_{32}O_9N_5Br$ requires C, 50·8; H, 4·9; N, 10·6; Br, 12·1%). Deacetylbromo-*N*-ethylstrychnospermine picrate gave the same colour reactions as did deacetyl-*N*-ethylstrychnospermine.

Oxidation of Demethylstrychnospermine by Means of Chromic Acid; Formation of apo*Spermostrychnine.*—Demethylstrychnospermine (7 g.), dissolved in water (150 c.c.) and concentrated sulphuric acid (50 c.c.), was slowly treated with a solution of chromic anhydride (18 g.) in water (20 c.c.) during ½ hr. The mixture was kept at room temperature for two days. The excess of chromic acid was then reduced with sulphur dioxide, which was in turn removed by boiling. The solution was made alkaline with barium hydroxide solution and filtered, and the precipitate washed with hot water. The combined filtrates (2 l.) were treated with just enough sulphuric acid to precipitate the barium as sulphate. After filtration the colourless solution was concentrated *in vacuo* to 10 c.c.; crystallisation then occurred. The solid (0·7 g.)

was collected, and more of the same substance (0·9 g.) was obtained on chloroform-extraction of the mother-liquor after neutralisation with sodium hydrogen carbonate. apo*Spermostrychnine* (III) crystallised from water in colourless prisms, m. p. 317—318° (decomp.), $[\alpha]_D^{18}$ −18° (*c*, 2·2 in H_2O) (Found, in material dried at the room temperature: C, 61·1; H, 7·5; N, 9·8; NMe, 2·75; *C*-Me, 6·9; loss at 100°, 7·1. Found, in material dried at 100°: C, 65·0; H, 7·6. $C_{18}H_{20}O_3N_2,H_2O$ requires C, 61·3; H, 7·6; N, 9·5; 1NMe, 9·9; 1*C*-Me, 5·1; $1H_2O$, 6·1. $C_{18}H_{20}O_3N_2$ requires C, 65·2; H, 7·3%). It did not give a colour reactions with oxidising agents or diazonium salts.

Action of Hydrogen Peroxide on apo*Spermostrychnine.*—A solution of the base (0·260 g.) in 3% hydrogen peroxide (1 c.c.) was mixed with one of barium hydroxide (0·35 g.) in water (10 c.c.), kept for an hour and then heated on a steam-bath for 10 min. The precipitated barium carbonate was collected and dried at 100° (Found: 0·170 g. of $BaCO_3$. Required: 0·173 g.). The filtrate was acidified with sulphuric acid, and sulphur dioxide passed through the boiling solution for 15 min. The excess of sulphur dioxide was expelled and barium hydroxide solution added until the sulphate ions were removed. The filtered aqueous solution was evaporated to dryness *in vacuo*, leaving a solid (0·22 g.), $[\alpha]_D^{20}$ −62° (*c*, 0·4 in H_2O), which was freely soluble in water giving an alkaline reaction, but was quite insoluble in ether or acetone. Neither this substance nor its perchlorate crystallised.

Distillation of Deacetylstrychnospermine over Zinc Dust.—The experiment was carried out using the apparatus described by Schmid, Ebnöther, and Karrer (*Helv. Chim. Acta*, 1950, **33**, 1486). Deacetylstrychnospermine (0·5 g.) was mixed with zinc dust (20 g.) and pyrolysed in quantities of 1—2 g. in a stream of hydrogen, the temperature of the furnace being raised to 450° at the end of each operation. The tubes were washed with ether and the washings added to the condensate. The ether extract was shaken with three portions of dilute hydrochloric acid to remove the basic fraction. The ethereal solution, after evaporation, left a residue with an indolaceous odour and giving a strong Ehrlich reaction, but no crystalline picrate could be obtained from it. The hydrochloric acid extract was basified and steam-distilled, and the distillate treated with solid potassium hydroxide and extracted with ether. The addition of ethereal picric acid to the dried extract gave a crop of crystals, which was recrystallised from a little alcohol, forming yellow needles (*ca.* 5 mg.), m. p. 115—120°, mixed m. p. with 3-ethylpyridine picrate [m. p. 127—128° (Karrer *et al.*, *loc. cit.*)] 115—122° (m. p. much depressed by admixture with picric acid) (Found: C, 46·7; H, 3·6. Calc. for $C_{13}H_{12}O_7N_4$: C, 46·5; H, 3·6%).

Attempted Cleavage of the Ether Ring of Strychnospermine.—The only product obtained from the reaction of 65% hydrobromic acid on strychnospermine at temperatures up to 150°, in a sealed tube, was deacetyldemethylstrychnospermine dihydrobromide. In other experiments, the above dihydrobromide (1 g.) was heated in a sealed tube with hydrobromic acid (20 c.c., saturated at −5°) at 150—160°. Evaporation of the mixture to dryness *in vacuo* gave a product containing some non-ionic bromine, but it was not obtained crystalline.

Spermostrychnine Methoperchlorate.—When perchloric acid was added to an aqueous solution of spermostrychnine methiodide colourless needles of the *perchlorate* were obtained, having m. p. 250° (decomp.) (Found: C, 59·0; H, 6·6; N, 6·7; Cl, 8·2. $C_{23}H_{29}O_6N_2Cl$ requires C, 58·6; H, 6·5; N, 6·2; Cl, 7·9%).

Deacetylspermostrychnine Hydriodide.—Sodium iodide was added to a solution of deacetylspermostrychnine in dilute hydrochloric acid. The *hydriodide* crystallised and was obtained as colourless, rectangular plates on recrystallisation from water. It did not melt, but blackened above 310° (Found: C, 52·6; H, 6·0; N, 6·5; I, 29·5. $C_{19}H_{25}ON_2I,\frac{1}{2}H_2O$ requires C, 52·7; H, 6·1; N, 6·5; I, 29·3%).

Deacetylformylspermostrychnine.—Deacetylspermostrychnine (0·1 g.) was heated with anhydrous formic acid (5 c.c.) for 1 hr. on the steam-bath. Dilution with water and addition of ammonia precipitated the *formylated base*, which crystallised from acetone in needles, m. p. 260° (decomp.), $[\alpha]_D^{18}$ ±0° (*c*, 2·0 in $CHCl_3$), $[\alpha]_D^{19}$ −66° (*c*, 1·45 in 0·1N-HCl) (Found: C, 74·5; H, 7·7. $C_{20}H_{24}O_2N_2$ requires C, 74·1; H, 7·5%). The Otto reaction (80% sulphuric acid) gave an intense reddish-violet colour, fading through deep red.

Oxidation of Spermostrychnine by Means of Chromic Acid.—A solution of chromic anhydride (2·5 g.) in water (10 c.c.) was gradually added to one of spermostrychnine (0·8 g.) in water (70 c.c.) and 96% sulphuric acid (10 c.c.), the temperature being kept near 60°. After 6 hr. at 60° the solution was allowed to cool overnight. The mixture was worked up as described for the oxidation of demethylstrychnospermine except that the excess of barium ions was removed with carbon dioxide. The product (0·15 g.) was recrystallised several times from water and then

had m. p. 320° (decomp.), unchanged on admixture with *apo*spermostrychnine, $[\alpha]_D^{20}$ −16° (*c*, 3·6 in H_2O) (Found: C, 60·9; H, 7·3. Calc. for $C_{15}H_{20}O_3N_2.H_2O$: C, 61·3; H, 7·6%). This base could also be termed *apo*strychnospermine since the benzene ring is removed in both cases and the methoxyl group of strychnospermine is the only feature of the molecule which is not reproduced in spermostrychnine.

Zinc Dust Distillation of Deacetylspermostrychnine.—This was carried out as described for deacetylstrychnospermine, but the hydrobromide (1 g.) was used instead of the free base, as otherwise a considerable quantity escaped pyrolysis by volatilisation. The basic fraction was obtained as before and gave a crystalline picrate, which when crystallised from alcohol–ether and then four times from methanol–ether had m. p. 121—123°, and mixed m. p. with 3-ethylpyridine picrate (m. p. 127—128°) 124—126° (Found: C, 47·2; H, 3·7. Calc. for $C_{13}H_{12}O_7N_4$: C, 46·5; H, 3·6%). The non-basic fraction was distilled in a microsublimation apparatus, giving first fractions, b. p. 110°/0·1 mm. and 150—160°/0·02 mm. The first fraction, which gave a strong Ehrlich reaction, was dissolved in benzene and treated with a solution of picric acid in the same solvent. Careful addition of light petroleum gave dark red crystals (25 mg.), m. p. 120—135°. Recrystallisation from benzene–light petroleum gave reddish-brown needles, m. p. 120—148°, unchanged on admixture with the picrate, of the same m. p., obtained from a synthetic mixture of 3-ethylindole (70%) and skatole (30%) (Wieland and Witkop, *Annalen*, 1947, **558**, 144; Karrer *et al.*, *loc. cit.*). The second fraction was chromatographed in benzene solution over alumina. The benzene eluate was evaporated to dryness and the residue on crystallisation from light petroleum (b. p. 40—60°) gave a minute amount of crystals, m. p. *ca.* 200°, which showed colour reactions typical of carbazole. The amount obtained was insufficient for further purification.

Spermostrychnine N-Oxide.—A mixture of spermostrychnine (0·5 g.), hydrogen peroxide (0·5 c.c. of 30%), and water (15 c.c.) was heated for 2 hr. on a steam-bath. A little platinum black was then added and the filtered solution evaporated to dryness. The crystalline residue of the *N*-oxide was recrystallised from acetone and had m. p. 241—243° after sintering at 190—200°. A solution of the *N*-oxide (0·05 g.) in water (2 c.c.) was heated at 100° with potassium chromate (0·005 g.). After 6 hr. only a small amount of precipitate had separated. The solution was filtered, but the substance did not crystallise. It dissolved readily in acids and gave an amorphous neutral compound with nitrous acid.

Deoxydihydrospermostrychnine.—Deacetylspermostrychnine dihydrobromide, prepared from the free base (0·2 g.) and dilute hydrobromic acid, was heated in a sealed tube with hydrogen bromide in acetic acid (30 c.c.; 50% w/v) at 180—200° for 2 hr. The solution obtained was concentrated to a small volume *in vacuo*, diluted with acetic acid (20 c.c.), and treated with zinc dust (5 g.) on a steam-bath for 4 hr. The mixture was filtered and the filtrate made strongly alkaline and then extracted thrice with ether. Evaporation of the extract left an oil, which was warmed with acetic anhydride (2 c.c.) for 30 min. on a steam-bath. The acetylated base was obtained in the usual way and converted into the crystalline *perchlorate*, which after four recrystallisations from aqueous perchlorate acid formed colourless needles (0·08 g.). The perchlorate softened at 117—118° and gradually melted, but it did not clear until 155°. The softening point rose considerably when the perchlorate was dried above room temperature [Found, in material dried at the room temperature: C, 55·8; H, 7·5; *C*-Me, 8·7, 8·3%; $[\alpha]_D^{22}$ +74° (*c*, 2·1 in 50% aqueous alcohol), +70° (*c*, 1·0 in the same solvent). In material dried at 117° *in vacuo*: C, 57·0; H, 7·0%; $[\alpha]_D^{19}$ +82° (*c*, 1·1 in 50% in aqueous alcohol). In material dried at 130° *in vacuo*: C, 59·7; H, 6·5. $C_{21}H_{28}ON_2.HClO_4.1\frac{1}{2}H_2O$ requires C, 55·8; H, 7·2; 3*C*-Me, 10·0. $C_{21}H_{28}ON_2.HClO_4.H_2O$ requires C, 51·0; H, 7·1. $C_{21}H_{28}ON_2.HClO_4$ requires C, 59·4; H, 6·9%]. The regenerated *base* did not crystallise. It was obtained as a colourless glass by distillation at 0·08 mm. (Found: C, 77·1; H, 8·9. $C_{21}H_{28}ON_2$ requires C, 76·8; H, 8·6%).

Preparation of the Wieland–Gumlich Aldehyde.—The following modification was found more convenient on a large scale, and to give better yields in the last step, than the original method (*loc. cit.*).

A suspension of finely-powdered strychnine (112 g.) in absolute alcohol (1 l.) and *iso*pentyl nitrite (200 c.c.) in a 5-l. flask fitted with a stirrer and an efficient condenser (jacket at −20°) was treated during several hours with a solution of sodium ethoxide prepared from absolute alcohol (1·5 l.) and sodium (31 g.). The temperature was kept at 70° during the addition, and for 4 hr. in all. The clear brown solution was concentrated to a small bulk *in vacuo* and mixed with water (1·5 l.). The mixture was acidified with acetic acid and the upper layer of *iso*pentyl alcohol separated. The alcohol was washed several times with dilute acetic acid and the combined aqueous solutions (*ca.* 2 l.) were treated with charcoal, filtered, and then made alkaline

with ammonia. The crystalline precipitate was collected, and washed with water, then with methanol, and finally with ether. The light brown powdery product (84 g.) was completely soluble in dilute alkali and acid.

The above hydroxyiminostrychnine was added to concentrated hydrochloric acid (22 c.c.) in water (500 c.c.). The solution was heated to boiling (charcoal), filtered, and allowed to cool. The hydrochloride formed large yellow needles, which dried at 100° to a yellowish powder (70 g.). The dry hydrochloride (20 g.) was slowly added to thionyl chloride (60 c.c.) at room temperature. When all the product had dissolved it was poured on ice with vigorous stirring, and then kept for some time, the precipitate becoming crystalline. The hydrochloride (17 g.) was collected and washed with methanol and then with ether. It was dissolved in hot water (400 c.c.) containing sodium acetate (10 g.), and the mixture vigorously boiled for 1½ hr., a stream of nitrogen being passed meanwhile. The cold solution was made alkaline with ammonia and extracted with chloroform. The carefully dried extract was concentrated *in vacuo* at as low a temperature as possible, leaving a residue which was triturated with a little acetone and collected. The product (5·7 g.) crystallised from pure chloroform in colourless prisms containing solvent of crystallisation. It showed no carbonyl band in its infrared spectrum.

Reduction of the Wieland–Gumlich Aldehyde; Formation of the Glycol (VI).—(a) *With lithium aluminium hydride.* A solution of the aldehyde (4 g., containing 1 mol. of chloroform) in pure tetrahydrofuran (80 c.c.) was added to a boiling suspension of lithium aluminium hydride (1·4 g.) in the same solvent (100 c.c.). The mixture was refluxed for 2 hr. and then kept overnight. The excess of reagent was decomposed with ethyl acetate, and the mixture shaken with 5% sodium hydroxide solution (50 c.c.). The tetrahydrofuran layer was quickly decanted from the lower aqueous solution and evaporated to dryness. The residue crystallised from aqueous alcohol in colourless prisms (2 g.) of the *base*, m. p. 251—253° (Found: C, 72·9; H, 7·9; N, 8·7. $C_{19}H_{24}O_2N_2$ requires C, 73·0; H, 7·7; N, 9·0%).

(b) *With potassium borohydride.* The aldehyde (4 g.) in 80% methanol (50 c.c.) was added to a solution of potassium borohydride (0·5 g.) in water (15 c.c.). The mixture was kept for ½ hr. and then diluted with water (20 c.c.), and the methanol boiled off. The Wieland–Gumlich glycol (VI) crystallised during the concentration and was collected (2·7 g.) after cooling of the solution; it had m. p. 251—253°, undepressed by admixture with the product prepared by method (a). The *dihydrochloride*, prepared by adding acetone to a solution of the base in dilute hydrochloric acid, formed colourless needles, m. p. 245—250° (decomp.; sintering at 240°), $[\alpha]_D^{20}$ −4° (*c*, 1·8 in H_2O) (Found: C, 56·7; H, 7·2; Cl, 18·3. $C_{19}H_{24}O_2N_2,2HCl,H_2O$ requires C, 56·7; H, 7·0; Cl, 17·6%).

Catalytic Hydrogenation of the Wieland–Gumlich Glycol (VI).—The compound, $C_{19}H_{24}O_2N_2$ (VI) (0·5 g.), in 50% aqueous acetic acid (30 c.c.) was hydrogenated in the presence of palladium chloride (0·15 g. in 10 c.c. of water and 2 c.c. of concentrated hydrochloric acid) and charcoal (1·5 g.). The mixture took up 85 c.c. of hydrogen (22°/760 mm.) during 1 hr., after which absorption ceased. The catalyst was collected and washed with hot water, and the combined filtrate made strongly alkaline with aqueous sodium hydroxide. The crystals (0·4 g.) were collected, and, after drying, had m. p. 170°. They were dissolved in a little dilute hydrochloric acid and the *dihydrochloride* precipitated with acetone. The salt was recrystallised several times from water (3—4 c.c.) by the addition of acetone to incipient opalescence, and was then obtained as colourless glistening needles, m. p. 260—265° (decomp.), $[\alpha]_D^{21}$ −3·3° (*c*, 2·5 in H_2O) (Found: C, 58·6; H, 7·4; Cl, 18·5; *C*-Me, 5·6. Found, in material dried for 5 hr. at 100° *in vacuo*: C, 58·8; H, 7·3. $C_{19}H_{26}O_2N_2,2HCl$ requires C, 58·9; H, 7·5; Cl, 18·3; 1*C*-Me, 3·9%). The regenerated *base* crystallised from methanol in prisms, m. p. 172—174° [Found, in material dried at the room temperature: C, 73·4; H, 8·3. In material dried at 100° for 5 hr.: C, 73·0; H, 8·3. In material sublimed *in vacuo*: C, 74·6, 72·9, 74·7, 74·5; H, 8·2, 8·6, 8·4, 8·4; *C*-Me, 6·3%; *M* (micro-Rast), 244. $C_{19}H_{26}O_2N_2$ requires C, 72·6; H, 8·4; 1*C*-Me, 4·8%; *M*, 314. $C_{19}H_{26}ON_2$ requires C, 76·5; H, 8·8; 1*C*-Me, 5·0%; *M*, 298. $C_{19}H_{24}ON_2,0·5H_2O$ requires C, 74·8; H, 8·2%].

Preparation of Dihydrodeoxyspermostrychnine (IV) *from Strychnine.*—The substance (0·15 g.) obtained by hydrogenation of the Wieland–Gumlich glycol (VI) as described above was heated in a sealed tube at 180—190° with hydrogen bromide in acetic acid (25 c.c.; 50% w/v) for 2 hr. The contents of the tube were worked up by reduction with zinc dust and reacetylation as described in the experiment on the cleavage of the ether ring of spermostrychnine. The perchlorate, after four crystallisations from water, formed colourless needles which softened at 117—118° and gradually melted, but did not form a clear liquid until 155°. This behaviour was unchanged on admixture with deoxydihydrospermostrychnine perchlorate. The salt

had $[\alpha]_D^{20}$ +78° (*c*, 1·0 in 50% aqueous alcohol) (Found: C, 56·2; H, 7·4. Calc. for $C_{21}H_{26}ON_2,HClO_4,1\frac{1}{2}H_2O$: C, 55·8; H, 7·1%).

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Liquid Metals. Part II. The Surface Tension of Liquid Sodium : the Drop-volume Technique.*

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The surface tension of liquid sodium in an atmosphere of pure argon has been measured over the temperature range 110—220° by a drop-volume method, which is described. The temperature coefficient of tension is −0·1 dyne cm.$^{-1}$ degree^{-1}, and extrapolation of results to the melting point of sodium gives $\gamma = 202$ dynes cm.$^{-1}$. Results are compared with those obtained by the vertical-plate method.

PART I * described the measurement of the surface tension of liquid sodium by the vertical-plate technique, with plates of zinc and copper and an atmosphere of pure argon. This method gave $\gamma = 195$ dynes cm.$^{-1}$ at the melting point of sodium (98°), with a temperature coefficient of −0·1 dyne cm.$^{-1}$ degree^{-1}. The method involves the exposure of the sodium surface to the argon atmosphere for periods of several minutes, but the value obtained agrees closely with the value 191 dynes cm.$^{-1}$ at 98° obtained by Taylor (A.E.R.E. Report M/R.1247, 1953; *J. Inst. Met.*, 1954—55, **83**, 143) using the maximum bubble-pressure method, so that there appear to be no errors resulting from contamination of the sodium surface. However, in view of the importance of this value in the study of the wetting of solids by liquid sodium, it was desirable to confirm the value of the tension by using a different method. In the first determination of the surface tension (Quincke, *Ann. Physik*, 1868, **135**, 621) the drop-weight technique was used, but the method has not been employed since then; it was therefore also of interest to ascertain to what extent the high value obtained by Quincke (252 dynes cm.$^{-1}$ at the melting point) was due to the use of carbon dioxide as an " inert " atmosphere.

EXPERIMENTAL

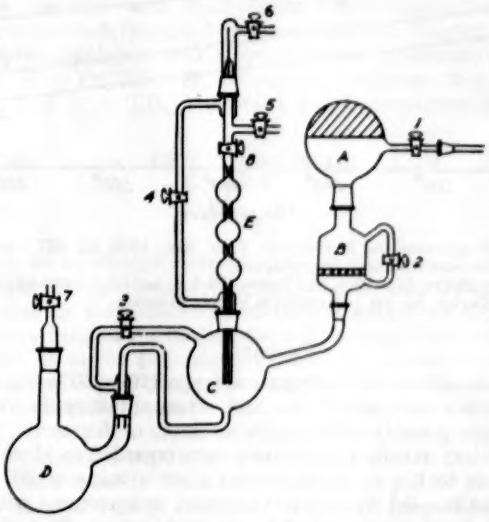
Purification of sodium and argon was carried out as described in Part I (*loc. cit.*). Values used for the density of sodium were also given therein. A diagram of the drop-volume apparatus used is shown in Fig. 1. It was constructed in Pyrex glass, the ground-glass joints being held in place by metal clips (not shown) to enable the apparatus to withstand an internal pressure of argon. Taps were lubricated with molybdenum disulphide (Ragosine Anti-scuffing powder). Silicone grease cannot be used in any part of the apparatus, since even traces of it have a considerable effect on the surface properties of liquid sodium : drops of the metal form irregularly on the orifice, and the apparent tension is reduced to as little as half of the true value. The apparatus consists essentially of a drop-volume pipette, with devices for filling the pipette with sodium through the orifice and for removing excess of sodium. The pipette *E* has three bulbs of known volume (each about 2 ml.). The orifice (internal radius 0·118 cm.) was prepared by making a small scratch on a capillary tube, and then breaking the tube to give a sharp edge; drop formation was more satisfactory from this type of orifice than from a ground orifice. Since clean sodium does not wet glass, the drops formed on the inside rim of the orifice, and the physical constants of the pipette were checked by determination of the interfacial tension of chlorobenzene and carbon tetrachloride against water, where the same conditions apply. When used for high-temperature measurements with sodium, the bulb volumes and orifice radius were corrected for thermal expansion of the glass. Surface tensions were calculated by the usual formula $\gamma = mgF/r$, the correction factor F being determined from the tables of Harkins and

* Part I, *J.*, 1954, 2861.

Brown (*J. Amer. Chem. Soc.*, 1919, **41**, 499). The orifice size used is near the lower practicable limit. Owing to the high surface tension of liquid sodium, there is a sharp change in internal pressure as a drop falls away; with small orifice diameters the drops were rapidly ejected from the orifice, the metal recoiled far into the orifice tube, and it was not possible to control drop formation adequately. The top of the pipette was drawn off to a fine thread, so that during an experiment the sodium flowed slowly from the bulbs under gravity.

Method.—The component parts of the apparatus were cleaned, dried at 200—250°, and assembled as in Fig. 1. The whole assembly was then placed inside a thermostatically controlled air-oven, with the argon lead to tap 1 passing through the side of the oven. The apparatus was then flushed with pure argon for 2 hr. at 0·5 l./min. To allow argon circulation, taps 1, 2, 3, 4, and 8 were kept open, and the gas was allowed to escape from taps 5, 6, and 7 in turn. This argon flow was continued throughout the experiment. With taps 2, 5, and 6 closed, the oven was raised to a temperature about 10—20° below that selected for the measurements. The sodium (previously purified) contained in flask *A* melted and flowed on to the glass sinter plate (grade 3, diam. 7 cm.) in the filter vessel *B*. When the plate was covered, argon pressure forced

FIG. 1.



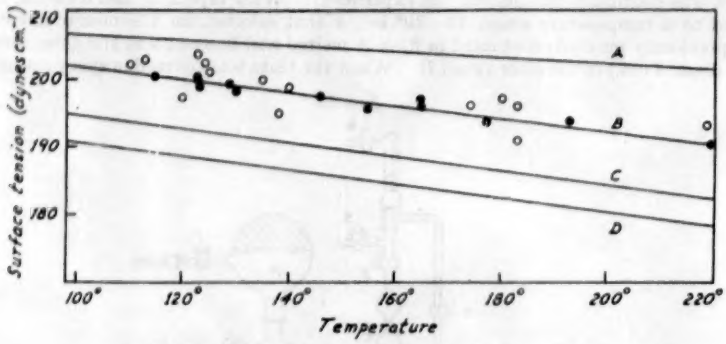
the sodium through the plate and into vessel *C*. This was continued until the sodium in *C* rose about 2 cm. above the orifice level; the flow of sodium was stopped by opening tap 2. The temperature of the oven was then raised to that at which the measurements were to be made. On closing taps 4 and 7, argon pressure increased in *C*, forcing sodium through the orifice into the bulbs of the pipette. When these were filled, tap 8 was closed and taps 4 and 7 were opened to release argon pressure. The sodium remaining in vessel *C* was removed by closing tap 3, a syphon being created between vessels *C* and *D*. The sodium flowed into *D*, leaving a clean orifice. When tap 8 was opened the sodium in the pipette flowed slowly under gravity, from the orifice, and the number of drops (about 20) obtained from each bulb was counted. By measuring the time of formation of each drop it was possible to calculate, with sufficient accuracy, the drop fractions formed as the sodium level passed the bulb calibration marks. Variation in times of drop formation produced no significant difference in the measured tension provided the time exceeded about 12 seconds. This is illustrated by the following data:

Time of drop formation (sec.)	32	47	140	180	240
γ (dynes cm.$^{-1}$)	198·5	198	199	199	198·5
Temperature	129°	130°	123°	123°	123°

Most of the results recorded in Fig. 2 were obtained at flow rates of about 60 sec. per drop. It was sometimes found possible to filter more sodium into *C*, to refill the pipette, and to repeat a measurement before dismantling the apparatus.

Dismantling Procedure.—The greatest risk of fire arises during the dismantling of the apparatus. Any sodium remaining in filtration unit *B* was transferred through the filter plate into vessel *C* by closing tap 2 for a short time. The sodium in *C* was then transferred into vessel *D* by closing tap 3. The apparatus was removed from the oven, the exit tube of vessel *D* removed, and the sodium poured into a steel mould by tilting the whole assembly; the argon flow was turned off, and vessel *D* quickly stoppered to prevent ingress of oxygen. When cool, the apparatus was dismantled, and the sodium removed by immersing the component parts in ethyl alcohol. Filtration unit *B* was cleaned with glacial acetic acid, since the sintered plate rapidly disintegrated in the presence of hot alcoholic sodium ethoxide solution.

FIG. 2.



A, Poindexter and Kernaghan, *Phys. Rev.*, 1929, **33**, 837 : sessile drop.
B, Present results : drop volume.
C, Addison, Kerridge, and Lewis, Part I, *loc. cit.* : vertical plate.
D, Taylor, *loc. cit.* : maximum bubble pressure.

RESULTS

Surface-tension values over the temperature range 110—220° are given in Fig. 2. The experimental routine is a complicated one and, when adjustments were made during an experiment which might possibly influence the accuracy of the results, the latter are shown in Fig. 2 as open circles; results from experiments regarded as ideal are shown as black points. Extrapolation to the m. p. of sodium gives a value of 202 dynes cm.$^{-1}$. The temperature coefficient is $-0{\cdot}1$ dynes cm.$^{-1}$ degree^{-1}, in agreement with the vertical plate results (line *C*) but the tension values are 7 dynes cm.$^{-1}$ higher. Part of this small difference may be attributable to the various correction factors necessary in each method, but the general agreement in the results shows that the drop-volume method, using a glass orifice, is acceptable for the determination of the surface tension of liquid sodium. If it is assumed that traces of sodium oxide on the metal surface are able to lower the surface tension, then it is to be expected that values determined by the drop-volume method, in which a fresh surface is continually formed, would be somewhat higher than with the vertical-plate method, in which the surface is exposed for longer periods. This aspect will be discussed in greater detail in a later paper on the influence of oxide films on the surface tension of liquid sodium.

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THE UNIVERSITY, NOTTINGHAM. [*Received, March 11th*, 1955.]

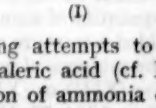
The Action of Ammonia on 4-Alkylidene-2-thiothiazolid-5-ones.

By F. P. Doyle, D. O. Holland, and J. H. C. Nayler.

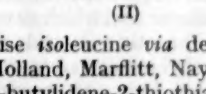
[Reprint Order No. 6041.]

In addition to the previously reported 5-substituted 2-thiothiazolidine-4-carboxyamides the action of ammonia on 4-alkylidene-2-thiothiazolid-5-ones gives acidic substances, sometimes as the major products, which on the basis of chemical and physical properties are formulated as 5-substituted tetrahydro-2-thioglyoxaline-4-thiocarboxylic acids.

The action of aqueous ammonia on 4-substituted-methylene-2-thiothiazolid-5-ones (I) in which one of the groups R and R′ is aromatic (either benzenoid or heterocyclic) is known to lead to 5-substituted 2-thiothiazolidine-4-carboxyamides (II) or to 5-arylidene-2-thiohydantoins (III) or a mixture of both (Chatterjee, Cook, Heilbron, and Levy, *J.*, 1948, 1337; Cook, Hunter, and Pollock, *J.*, 1950, 1892; Holland and Nayler, *J.*, 1953, 285). The corresponding reaction with 4-alkylidene-2-thiothiazolid-5-ones (I; R = alkyl, R′ = H or alkyl) has been less thoroughly studied but Cook, Hunter, and Pollock (*loc. cit.*) reported that the 4-*iso*propylidene and 4-*iso*butylidene compounds gave the amides (II; R = R′ = Me, and R = Pr^i, R′ = H, respectively) whereas 4-*cyclo*pentylidene-2-thiothiazolid-5-one (I; R + R′ = $[CH_2]_4$) afforded 5-*cyclo*pentylidene-2-thiohydantoin (III; R + R′ = $[CH_2]_4$).



(I)



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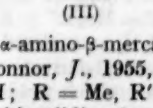
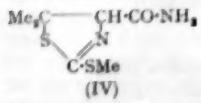


(III)

During attempts to synthesise *iso*leucine *via* derivatives of α-amino-β-mercapto-β-methylvaleric acid (cf. Doyle, Holland, Marflitt, Nayler, and O'Connor, *J.*, 1955, 1719), the action of ammonia on 4-*sec.*-butylidene-2-thiothiazolid-5-one (I; R = Me, R′ = Et) was found to give very little of the desired 5-ethyl-5-methyl-2-thiothiazolidine-4-carboxyamide (II; R = Me, R′ = Et) but yielded mainly an isomeric acidic product which appeared to be a mixture of two forms (see p. 2267). When the reaction was applied to 4-*iso*propylidene-2-thiothiazolid-5-one (I; R = R′ = Me), thus avoiding *cis-trans*-isomerism, only about 1% of 5 : 5-dimethyl-2-thiothiazolidine-4-carboxyamide (II; R = R′ = Me), m. p. 178—179°, identical with a specimen prepared from the corresponding methyl ester and ammonia, was obtained. The major product, m. p. 151° (decomp.), was isomeric with the amide (II; R = R′ = Me), and similar in general properties to the acidic product from the *sec.*-butylidene derivative. Similar results were obtained whether hot aqueous or cold alcoholic ammonia was used. Cook, Hunter, and Pollock (*loc. cit.*) reported only one product, m. p. 145°, from the reaction of 4-*iso*propylidene-2-thiothiazolid-5-one with ammonia, which they considered to be the amide (II; R = R′ = Me). This with methyl sulphate and potassium hydroxide gave a compound, m. p. 206°, which was assumed by these workers to be the *S*-methyl derivative (IV) although it did not give 5 : 5-dimethylthiazolidine-4-carboxyamide on reaction with aluminium amalgam. Cook *et al.* (*loc. cit.*) considered the latter reagent had caused isomerisation although the m. p. of the product (200°) was not depressed by admixture with the starting material. It appears likely, however, that the compound, m. p. 145°, was identical with our acid, m. p. 151° (decomp.), since the latter with methyl sulphate and alkali gave a methyl ester, m. p. 206°, which was unchanged by prolonged heating with aluminium amalgam.

The compound, m. p. 151° (decomp.), when heated with aqueous mineral acid yielded an acid, $C_6H_{10}O_2N_2S$, in which a thiol group had been replaced by hydroxyl. Cold methanolic or ethanolic hydrogen chloride effected a similar replacement to give a methyl and an ethyl ester, respectively. Both the latter ester and the methyl ester (m. p. 206°) on mild alkaline hydrolysis also gave the same acid $C_6H_{10}O_2N_2S$. These reactions indicated the presence of a thiocarboxyl group in the acid, m. p. 151° (decomp.). Of the possible structures (VI, VII, and VIII; R = R′ = Me) containing such a grouping (VI) appeared

to be unlikely since it would have been expected to cyclise either to the thiazolidone (I; R = R′ = Me) or, more probably, to the thiohydantoin (III; R = R′ = Me) on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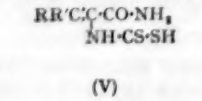
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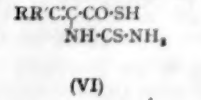
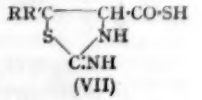
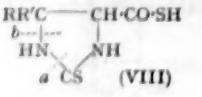
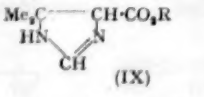

(VI)


(VII)

treatment with mineral acid. The structure (V) would likewise have been expected to revert to the thiazolidone.

Of the remaining structures (VII and VIII; R = R′ = Me) evidence against the former was obtained by the action of Raney nickel on the derived acid, $C_6H_{10}O_2N_2S$. Behringer and Zillikens (*Annalen*, 1951, **574**, 140) found that 2-aminothiazoline-4-carboxylic acid, which is unaffected by mineral acid, yielded alanine when reduced by Raney nickel. The acid, $C_6H_{10}O_2N_2S$, under these conditions, however, lost only a sulphur atom to give a product, $C_6H_{10}O_2N_2$, which was tentatively formulated as the dihydroglyoxaline (IX or X; R = H): the acid $C_6H_{10}O_2N_2S$ would thus have the structure (XI; R = R′ = Me, R″ = H) and the original compound the structure (VIII; R = R′ = Me). The ester (XI; R = R′ = Me, R″ = Et) was also desulphurised with Raney nickel to give (IX or X; R = Et), isolated as a picrate.


(VIII)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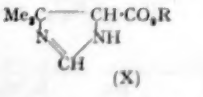
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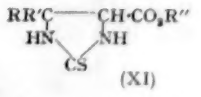
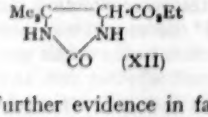
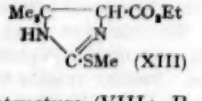

(XI)

Further support for structures (VIII—XI) was obtained by the action on the ester (XI; R = R′ = Me, R″ = Et) of (i) chloroacetic acid which gave a small quantity of a compound, $C_8H_{14}O_3N_2$, considered to be (XII), (ii) acetic anhydride which yielded a mixture of mono- and di-acetyl derivatives, and (iii) methyl iodide in dry acetone in the presence of potassium carbonate which yielded a basic methyl derivative, considered to be (XIII) or (XIV).

It appears from Baer and Lockwood's work (*J. Amer. Chem. Soc.*, 1954, **76**, 1162) that 2-alkylthiodihydroglyoxalines are more stable towards alkali than are acyclic *S*-alkyl*iso*-thioureas, and it was indeed found that brief heating of the substance (XIII or XIV) with aqueous sodium hydroxide gave no methanethiol and more prolonged treatment in the cold caused hydrolysis of the ester group only.


(XII)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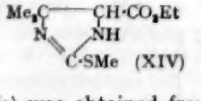
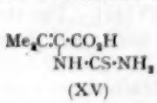

(XIV)

Further evidence in favour of structure (VIII; R = R′ = Me) was obtained from a comparison of ultraviolet spectra. This acid, the derived acid $C_6H_{10}O_2N_2S$, and the esters of both compounds all have an absorption maximum at 241—244 mμ, as have tetrahydro-2-thioglyoxaline, thiourea, and thiohydantoic acid. The presence of a carbon–carbon double bond as in (VI) would be expected to lead to a spectrum appreciably different from that of thiohydantoic acid since the spectrum of 5-*iso*propylidene-2-thiohydantion is quite unlike that of 2-thiohydantoin. Although Baer and Lockwood (*loc. cit.*) report $\lambda_{max.}$ 222 mμ (ε 10,500) for 2-*n*-butylthio-Δ^1-dihydroglyoxaline hydrochloride, neither dihydro-5 : 5-dimethyl-2-methylthioglyoxaline-4-carboxylic acid hydrochloride nor dihydro-2-methylthio-Δ^1-glyoxaline hydriodide showed ultraviolet absorption maxima at wavelengths greater than 210 mμ. Chemical evidence against an unsaturated acyclic structure was provided by the recovery of the acid (XI; R = R′ = Me, R″ = H) after attempted reduction with zinc and boiling acetic acid for 1 hr. or red phosphorus, iodine, and boiling moist acetic acid for 7 hours (cf. Miescher and Billeter, *Helv. Chim. Acta*, 1939, **22**, 601); treatment with sodium in liquid ammonia yielded no tractable product.

An alternative synthesis of the acid (XI; R = R′ = Me, R″ = H) *via* αβ-diamino-*iso*valeric acid failed when treatment of αβ-dibromo*iso*valeric acid with ammonia or potassium phthalimide yielded only 1-bromo*iso*butene (cf. Massot, *Ber.*, 1894, **27**, 1226; Farrell

and Bachman, *J. Amer. Chem. Soc.*, 1935, **57**, 1281). When ethyl αβ-dibromo*iso*valerate was heated with ethanolic ammonia under pressure no definite organic product could be isolated.

Attempts to prepare ββ-dimethyl-α-thioureidoacrylic acid (XV) for comparison with the acid, $C_6H_{10}O_2N_2S$, were also unsuccessful. When 5-*iso*propylidene-2-thiohydantoin (III; R = R′ = Me), which was readily prepared from acetone and 2-thiohydantoin, was heated with dilute alkali the *iso*propylidene group was cleaved, to yield thiohydantoic acid. The structure of 5-*iso*propylidene-2-thiohydantoin was confirmed by heating it with aqueous chloroacetic acid to give 5-*iso*propylidenehydantoin which in turn was catalytically hydrogenated to 5-*iso*propylhydantoin. Another attempt was made to prepare the unsaturated acid (XV) by a method similar to that used for α-acetamido-ββ-dimethylacrylic acid (" The Chemistry of Penicillin," Oxford Univ. Press, 1949, p. 465). A mixture of dimethylpyruvic acid and thiourea was heated under reduced pressure, but no ββ-dimethyl-α-thioureidoacrylic acid was obtained. Instead, 5-*iso*propylidenehydantoin was isolated, together with two unidentified compounds.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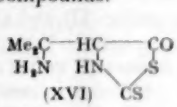
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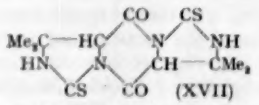
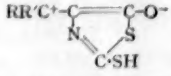
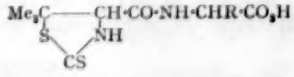

(XVII)

When tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-thiocarboxylic acid (VIII; R = R′ = Me) was heated for a short time in acetic acid, it gave 4-*iso*propylidene-2-thio-5-thiazolidone (I; R = R′ = Me) in 33% yield. Neither its methyl ester nor the derived carboxylic acid (XI; R = R′ = Me, R″ = H) underwent a comparable rearrangement. The thiazolidone could have arisen from (VIII; R = R′ = Me) either by ring opening at (*a*) and loss of ammonia from the amine (XVI) or *via* the acid (VI; R = R′ = Me) after cleavage at (*b*), although in the latter case the thiohydantoin (III; R = R′ = Me) would have been a probable product. Evidence for the former possibility was sought by including acetic anhydride in the reaction in the hope of isolating the acetyl derivative of the hypothetical intermediate (XVI), but neither it nor the thiazolidone (I; R = R′ = Me) was obtained. Instead, an acetyl derivative of the original acid was formed together with a neutral compound of empirical formula $C_6H_8ON_2S$. Both compounds apparently retained the tetrahydro-2-thioglyoxaline nucleus since each gave tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-carboxylic acid on hydrolysis. The acidic acetyl derivative also yielded the ethyl ester (XI; R = R′ = Me, R″ = Et) when treated with cold ethanolic hydrogen chloride. The neutral product, which was also obtained in small yield when the thio-acid was heated with acetic anhydride alone, is tentatively formulated as the diketopiperazine (XVII).

(XVIII) 


(XIX)

The action of ammonia on 4-*sec.*-butylidene-2-thio-5-thiazolidone (I; R = Me, R′ = Et) gave a very small yield of 5-ethyl-5-methyl-2-thiothiazolidine-4-carboxyamide (II; R = Me, R′ = Et), which on hydrolysis afforded the corresponding acid (which is known), but the main product appeared to be a mixture of the geometrical isomers of 5-ethyl-tetrahydro-5-methyl-2-thioglyoxaline-4-thiocarboxylic acid (VIII; R = Me, R′ = Et). Crystallisation of the acidic mixture gave only a small quantity of one isomer (arbitrarily designated the β-form); attempted separation of the phenethylamine salts was not successful. However, when the mixed acids were kept for 24 hours in aqueous sodium hydroxide and then acidified, the α-form resulted, and subsequent reactions were carried out either on this form or on the mixed isomers. Results paralleled those in the dimethyl series and the α-isomers of methyl 5-ethyltetrahydro-5-methyl-2-thioglyoxaline-4-thiol-carboxylate and of the esters (XI; R = Me, R′ = Et, R″ = Me and Et) were obtained without difficulty. Treatment of the mixed isomers of the thio-acid with ethanolic hydrogen chloride afforded chiefly the β-form of ethyl 5-ethyltetrahydro-5-methyl-2-thioglyoxaline-4-carboxylate. The two isomers of the ester (XI; R = Me, R′ = R″ = Et)

yielded the two isomeric acids when hydrolysed with sodium hydroxide in the cold, which contrasts with the apparent inversion of the β-form of the thio-acid under similar conditions.

The ratio of neutral to acidic products obtained by the action of ammonia on 4-alkylidene-2-thiothiazolid-5-ones (I) in which one of the groups R and R′ was hydrogen differed markedly from that when both groups were alkyl. Thus we confirm Cook, Hunter, and Pollock's observation (*loc. cit.*) that the main product from 4-*iso*butylidene-2-thiothiazolid-5-one (I; R = Pr^i, R′ = H) is 5-*iso*propyl-2-thiothiazolidine-4-carboxyamide (II; R = Pr^i, R′ = H), but a very small quantity of tetrahydro-5-*iso*propyl-2-thioglyoxaline-4-thiocarboxylic acid (VIII; R = Pr^i, R′ = H) was also isolated. Ammonia and 4-ethylidene-2-thiothiazolid-5-one (I; R = Me, R′ = H) gave 5-methyl-2-thiothiazolidine-4-carboxyamide (II; R = Me, R′ = H) together with a little acidic gum which was considered to contain the thio-acid (VIII; R = Me, R′ = H) since in hot acetic acid it reverted to 4-ethylidene-2-thiothiazolid-5-one.

The behaviour of 4-*cyclo*pentylidene- and 4-*cyclo*hexylidene-2-thio-5-thiazolidones towards ammonia was intermediate between that of the mono- and di-alkyl types, each giving substantial quantities of both the amide (II) and the thio-acid (VIII). The structures of the former were confirmed by hydrolysis to the corresponding acids, and those of the latter by reconversion into the thiazolidones (I) in hot acetic acid. The case of 4-*cyclo*pentylidene-2-thio-5-thiazolidone was of particular interest since we obtained none of the compound, m. p. 252° (decomp.), which Cook, Hunter, and Pollock (*loc. cit.*) reported as their sole product and considered to be 5-*cyclo*pentylidene-2-thiohydantoin (III; R + R′ = $[CH_2]_4$). A specimen of the latter which we prepared from 2-thiohydantoin and *cyclo*pentanone had m. p. 319° (decomp.).

It appears from the above results that the formation of 5-substituted tetrahydro-2-thioglyoxaline-4-thiocarboxylic acids (VIII) as well as the previously reported 5-substituted 2-thiothiazolidine-4-carboxyamides (II) by the action of ammonia on 4-alkylidene-2-thiothiazolid-5-ones of type (I) is quite general, but there remains no evidence of the formation of 5-alkylidene-2-thiohydantoins (III) in this way. It is not clear whether the tetrahydroglyoxalines are formed by way of the hypothetical unsaturated thio-acids (VI) or by an initial nucleophilic attack by the ammonia on the alkylidene group of the thiazolidone (I), possibly reacting in the form (XVIII).

The reaction of 4-*iso*propylidene-2-thiothiazolid-5-one with ammonia to give chiefly tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-thiocarboxylic acid is in marked contrast to its behaviour with the sodium salts of glycine or alanine, where the products are the peptide precursors (XIX; R = H or Me) (Cook and Pollock, *J.*, 1950, 1898; unpublished work from these laboratories). It was hoped that the inclusion of a strong base in the ammonia reaction would increase the yield of 5 : 5-dimethyl-2-thiothiazolidine-4-carboxyamide (II; R = R′ = Me), but in fact in the presence of 1 equiv. of sodium hydroxide or 3 equivs. of triethylamine the main product was still the thio-acid (VIII; R = R′ = Me).

Experimental

Preparation of 4-Alkylidene-2-thio-5-thiazolidones.—4-*iso*Propylidene-, 4-ethylidene-, and 4-*iso*butylidene-2-thio-5-thiazolidones were prepared as described by Billimoria and Cook (*J.*, 1949, 2323), and Doyle, Holland, Marflitt, Nayler, and O'Connor's method (*loc. cit.*) was used for 4-*sec.*-butylidene-2-thiothiazolid-5-one. 4-*cyclo*Pentylidene- and 4-*cyclo*hexylidene-2-thio-5-thiazolidones were prepared from 2-thio-5-thiazolidone and the appropriate ketones in the presence of zinc chloride (cf. Cook and Pollock, *J.*, 1949, 3007).

Reaction of 4-Alkylidene-2-thiothiazolid-5-ones with Ammonia.—(*a*) A mixture of the thiazolidone (I) (20 g.) and aqueous ammonia (*d* 0·88; 130 ml.) was heated on the steam-bath for 30—60 min. and the clear solution was cooled and strongly acidified with hydrochloric acid to precipitate a pale solid or gum. (In the case of 4-*cyclo*pentylidene-2-thio-5-thiazolidone part of the neutral product separated from the hot solution before acidification, whilst the products from 4-ethylidene-2-thio-5-thiazolidone were water-soluble and were extracted from the acidified solution with ethyl acetate.) The solid or gum was suspended in water and treated with sodium hydrogen carbonate until effervescence ceased. The crude 5-substituted 2-thiothiazolidine-4-carboxyamide (II) was collected and washed with water: details of the purification of individual compounds are given in Table 1. Acidification of the filtrate precipitated the crude

5-substituted tetrahydro-2-thioglyoxaline-4-thiocarboxylic acid (VIII), which frequently separated as a gum in the first instance : the individual acids are recorded in Table 2.

TABLE 1. *5-Substituted 2-thiothiazolidine-4-carboyxamides* (II).

Starting material (I)	Yield (%)	Cryst. form and solvent	M. p.	Formula	Found (%) C	H	N	Required (%) C	H	N
R = R′ = Me	{1 {1 *	Needles, H_2O	178—179°	$C_6H_{10}ON_2S_2$	38·1	5·2	—	37·9	5·3	—
R = Me, R′ = Et	{1 {3 *	Plates, H_2O	195—196	$C_7H_{12}ON_2S_2$	41·4	5·8	13·2	41·2	5·9	13·7
R = Me, R′ = H	17	Microcrystals, aq. EtOH	179—181	$C_5H_8ON_2S_2$	34·0	4·5	15·8	34·1	4·6	15·9
R = Pr^i, R′ = H	55	Needles, H_2O	156—157 †	$C_7H_{12}ON_2S_2$	41·5	5·8	13·9	41·2	5·9	13·7
R + R′ = $[CH_2]_4$	70	Prisms, EtOAc	168—169	$C_8H_{12}ON_2S_2$	45·2	6·0	13·2	44·4	5·6	12·9
R + R′ = $[CH_2]_5$	28	Needles, EtOH	211—212	$C_9H_{14}ON_2S_2$	47·4	6·2	11·8	46·9	6·1	12·2

* Method (*b*) used for preparation; in all other cases method (*a*) was used. † Cook, Hunter, and Pollock (*loc. cit.*) give m. p. 131°.

TABLE 2. *5-Substituted tetrahydro-2-thioglyoxaline-4-thiocarboxylic acids* (VIII).

Starting material (I)	Yield (%)	Cryst. form (from EtOH)	M. p. (decomp.)	Formula	Found (%) C	H	N	Required (%) C	H	N
R = R′ = Me	56	Prisms	151°	$C_6H_{10}ON_2S_2$	38·3	5·4	14·9	37·9	5·3	14·7
	69 *	—	—	—	—	—	—	—	—	—
R = Me, R′ = Et	56 †	—	—	—	—	—	—	—	—	—
	38 †	—	—	—	—	—	—	—	—	—
R = Me, R′ = H	Small ‡	—	—	—	—	—	—	—	—	—
R = Pr^i, R′ = H	1	Powder	176—177	$C_7H_{12}ON_2S_2$	41·2	6·0	13·8	41·2	5·9	13·7
R + R′ = $[CH_2]_4$	13	Needles	Indef. >180°	$C_8H_{12}ON_2S_2$	44·7	5·7	12·5	44·4	5·6	12·9
R + R′ = $[CH_2]_5$	67	Needles	Indef. >210°	$C_9H_{14}ON_2S_2$	47·3	6·0	11·9	46·9	6·1	12·2

* See footnote * to Table 1. † Mixture of isomers : isolation of the pure components is described later. ‡ Obtained only as a crude gum which, when heated in acetic acid, gave 4-ethylidene-2-thio-5-thiazolidone, m. p. and mixed m. p. 196° (decomp.).

(*b*) A suspension of the thiazolidone (I) (20 g.) in methanol (200 ml.) was saturated with ammonia and the resulting solution was kept at room temperature for 48 hr., then evaporated *in vacuo*. The residue was treated with dilute hydrochloric acid and worked up as in (*a*).

The four pure thio-acids listed in Table 2 all had an absorption maximum at 244 mμ (ε 17,350) in EtOH (cf. thiourea, $\lambda_{max.}$ 242 mμ, ε 12,780, tetrahydro-2-thioglyoxaline, $\lambda_{max.}$ 241 mμ, ε 16,500, and thiohydantoic acid, $\lambda_{max.}$ 242 mμ, ε 13,710).

Methyl Tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-thiolcarboxylate.—A solution of tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-thiocarboxylic acid (4 g.) in N-potassium hydroxide (30 ml.) was shaken with methyl sulphate (2·5 ml.) and after 90 min. the *methyl ester* (3·04 g., 71%) was collected and crystallised from water or aqueous alcohol as colourless needles, m. p. 206° (Found : C, 41·6; H, 5·8; N, 13·4. $C_7H_{12}ON_2S_2$ requires C, 41·2; H, 5·9; N, 13·7%). Absorption : $\lambda_{max.}$ 244 mμ, ε 18,000 in EtOH.

Methyl Tetrahydro-5 : 5-pentamethylene-2-thioglyoxaline-4-thiolcarboxylate.—The thio-acid (VIII; R + R′ = $[CH_2]_4$) was methylated with methyl sulphate and alkali as above; the *ester* (66%), crystallised from ethanol, had m. p. 217° (decomp.) (Found : C, 49·1; H, 6·6; N, 11·4. $C_{10}H_{16}ON_2S_2$ requires C, 49·1; H, 6·6; N, 11·5%).

Tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-carboxylic Acid.—(*a*) The thio-acid (VIII; R = R′ = Me) (2 g.) in 5N-hydrochloric acid (20 ml.) was refluxed for 90 min., then cooled to 0°. The hydrated *acid* (XI; R = R′ = Me, R″ = H) (1·38 g., 68%) was collected and crystallised from water in colourless prisms, m. p. 185—186° (Found : C, 37·4; H, 6·4; N, 15·1; S, 16·4. $C_6H_{10}O_2N_2S,H_2O$ requires C, 37·5; H, 6·3; N, 14·6; S, 16·7%). Absorption : $\lambda_{max.}$ 242·5 mμ, ε 16,600 in EtOH.

(*b*) The thio-acid (13 g.), suspended in dry ethanol (130 ml.), was saturated with hydrogen chloride at 0°, and the resulting solution was kept at room temperature for 24 hr. The solution was evaporated *in vacuo* and the residue was triturated with sodium hydrogen carbonate solution to yield *ethyl tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-carboxylate* (11·37 g., 82%) which, crystallised from benzene, had m. p. 102—104° (Found : C, 47·3; H, 7·1; N, 14·3; S, 15·9. $C_8H_{14}O_2N_2S$ requires C, 47·5; H, 7·0; N, 13·9; S, 15·9%). Absorption : $\lambda_{max.}$

242·5 mμ, ε 18,450 in EtOH. The *methyl ester*, similarly prepared in 71% yield and crystallised from ethyl acetate, had m. p. 173—174° (Found: C, 44·5; H, 6·3; N, 15·0. $C_7H_{12}O_2N_2S$ requires C, 44·7; H, 6·4; N, 14·9%).

The ethyl ester (7 g.) in alcohol (35 ml.) was treated with 5N-aqueous sodium hydroxide (35 ml.) and set aside for 48 hr. Removal of the alcohol *in vacuo* and acidification of the residue gave the hydrated acid (5·83 g., 88%), identical with the product from (*a*). Hydrolysis of methyl tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-thiolcarboxylate in a similar manner gave the same acid (80%).

Dihydro-5 : 5-dimethylglyoxaline-4-carboxylic Acid.—A solution of tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-carboxylic acid monohydrate (2 g.) in hot water (50 ml.) was refluxed for 4 hr. with Raney nickel, added in two portions. After removal of the nickel, the filtrate was evaporated *in vacuo*, and the residual gum was taken up in alcohol, and the evaporation repeated. The sticky greenish-blue residue was washed with alcohol–ether, and then with alcohol alone, to leave *dihydro-5 : 5-dimethylglyoxaline-4-carboxylic acid* as a white powder (0·81 g.) which crystallised from water–alcohol as needles of the monohydrate, m. p. 191—192° (decomp.) (Found: C, 45·0; H, 7·5; N, 17·3. $C_6H_{10}O_2N_2.H_2O$ requires C, 45·0; H, 7·6; N, 17·5%). The compound gave no colour with ninhydrin.

Reactions of Ethyl Tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-carboxylate.—(a) *With Raney nickel.* The ester (3 g.) in ethanol (30 ml.) was refluxed for 4 hr. with Raney nickel, added in two portions. After removal of the nickel, the filtrate was evaporated *in vacuo* to a green water-soluble gum which did not crystallise. A solution of the gum in warm ethanol was treated with picric acid (7 g.) in the same solvent and the yellow crystals which separated on cooling were collected (3·02 g.). *4-Ethoxycarbonyldihydro-5 : 5-dimethylglyoxaline picrate* crystallised from alcohol in yellow plates, m. p. 207° (Found: C, 42·2; H, 4·2; N, 17·8. $C_{14}H_{17}O_9N_5$ requires C, 42·1; N, 17·5%).

(b) *With chloroacetic acid.* A mixture of the ester (2 g.), chloroacetic acid (3 g.), and water (15 ml.) was refluxed for 2 hr., cooled, and neutralised with sodium hydrogen carbonate. The solution was evaporated *in vacuo*, and the residue extracted with hot ethyl acetate. Evaporation of the extracts gave a gum which afforded a white powder (0·19 g.) when rubbed with ether. *Ethyl tetrahydro-5 : 5-dimethyl-2-oxoglyoxaline-4-carboxylate* (XII) crystallised from ethyl acetate in needles, m. p. 157—158° (Found: C, 51·2; H, 7·7; N, 14·4. $C_8H_{14}O_3N_2$ requires C, 51·6; H, 7·6; N, 15·0%).

(c) *With acetic anhydride.* The ester (3 g.) in acetic anhydride (20 ml.) was refluxed for 16 hr., and the solution evaporated *in vacuo*. The residual solid was washed with water, dried, and boiled with light petroleum (50 ml., b. p. 60—80°). The insoluble residue (0·69 g.) was collected and crystallised from alcohol to give colourless needles of the *monoacetyl derivative*, m. p. 213—214° (Found: C, 49·5; H, 6·7; N, 11·1; S, 12·3. $C_{10}H_{16}O_3N_2S$ requires C, 49·2; H, 6·6; N, 11·5; S, 13·1%). Concentration of the petroleum extracts afforded the *diacetyl derivative* (2·58 g.), which crystallised from the same solvent in colourless prisms, m. p. 62—63° (Found: C, 50·6; H, 6·2; N, 9·6; S, 11·1. $C_{12}H_{18}O_4N_2S$ requires C, 50·3; H, 6·3; N, 9·8; S, 11·2%).

(d) *Methylation.* A mixture of the ester (30·3 g.), dry acetone (150 ml.), potassium carbonate (20·7 g.), and methyl iodide (10·5 ml.) was refluxed with stirring for 4 hr., cooled, and filtered. The solvent was removed *in vacuo* and the residual oil was triturated with light petroleum to give a white solid (29·3 g., 90%). *Ethyl dihydro-5 : 5-dimethyl-2-methylthioglyoxaline-4-carboxylate* crystallised from light petroleum in sheaves of rhombic plates, m. p. 75—77° (Found: C, 50·0; H, 7·3; N, 12·7. $C_9H_{16}O_2N_2S$ requires C, 50·0; H, 7·5; N, 13·0%). The base was stable to distillation (b. p. 91°/0·2 mm.).

Dihydro-5 : 5-dimethyl-2-methylthioglyoxaline-4-carboxylic Acid Hydrochloride.—A solution of the foregoing ester (3·7 g.) in alcohol (18 ml.) was treated with aqueous 5N-sodium hydroxide (18 ml.), set aside at room temperature for 24 hr., acidified with hydrochloric acid, and evaporated *in vacuo*. The residue was dried in a vacuum-desiccator (KOH) and extracted with several portions of hot ethanol. Evaporation of the extracts left a gum which crystallised when rubbed with ethyl acetate–methanol (5 : 1). The *hydrochloride* (2·71 g.) crystallised from ethanol–ethyl acetate in colourless rosettes, m. p. 183—185° (decomp.) (Found: C, 37·3; H, 5·8; N, 12·7. $C_7H_{13}O_2N_2SCl$ requires C, 37·4; H, 5·8; N, 12·5%).

5-iso*Propylidene-2-thiohydantoin.*—A mixture of 2-thiohydantoin (15 g.), acetone (40 ml.), and piperidine (40 ml.) was refluxed for 1 hr., poured into water (700 ml.), and acidified. 5-*iso*-Propylidene-2-thiohydantoin (17·9 g.) was collected and crystallised from alcohol (charcoal) in colourless needles, m. p. 261° (decomp.) (Found: C, 45·9; H, 4·9; N, 18·0. Calc. for $C_6H_8ON_2S$:

C, 46·1; H, 5·2; N, 17·9%). Dupré, Hems, and Robinson (Committee for Penicillin Synthesis Report No. 38) give m. p. 258°. Absorption : $\lambda_{max.}$ 238, 269·5, 327 mμ, ε 5320, 6530, 28,300 in EtOH (cf. 2-thiohydantoin : $\lambda_{max.}$ 220, 264 mμ, ε 10,000, 18,050).

Hydrolysis of 5-iso*Propylidene-2-thiohydantoin.*—The thiohydantoin (4 g.) in 10% sodium hydroxide solution (40 ml.) was refluxed for 30 min., cooled, and acidified. After 2 hr. at 0° the colourless crystals were collected, and concentration of the mother-liquor afforded a further crop of thiohydantoic acid (2 g. in all). It formed prismatic needles (from water), m. p. 172—173° (decomp.) [lit., m. p. 170—171° (decomp.)] (Found : C, 27·3; H, 4·7. Calc. for $C_3H_6O_2N_2S$: C, 26·9; H, 4·5%). With boiling 2N-hydrochloric acid the acid afforded 2-thiohydantoin (82%), m. p. and mixed m. p. 230—231° (decomp.). When 5-*iso*propylidene-2-thiohydantoin (1 g.) was boiled with barium hydroxide octahydrate (3 g.) in water (50 ml.) for 15 min., cooled and acidified, 0·15 g. was recovered unchanged together with 0·26 g. of thiohydantoic acid.

5-iso*Propylidenehydantoin.*—A suspension of 5-*iso*propylidene-2-thiohydantoin (3 g.) in 20% aqueous chloroacetic acid (20 ml.) was refluxed for 45 min., during which the thiohydantoin gave place to longer crystals of the hydantoin. The mixture was cooled and 5-*iso*propylidenehydantoin (2·36 g.) was collected. It formed fine colourless needles (from alcohol), m. p. 274° (decomp.) not depressed by admixture with a specimen prepared from acetone and hydantoin in piperidine at 130° (Boon, Carrington, and Jones, Committee for Penicillin Synthesis Report No. 20). We thus confirm the m. p. given by Boon *et al.* and by Tatsuoka and Miyamoto (*J. Pharm. Soc. Japan*, 1949, **69**, 294), whereas the values of 240° (decomp.) and 245° (decomp.) are quoted in Committee for Penicillin Synthesis Report No. 237 and by Cook, Heilbron, and Hunter (*J.*, 1949, 1443).

5-iso*Propylhydantoin.*—A solution of 5-*iso*propylidenehydantoin (2·1 g.) in dilute sodium hydroxide (pH 10) was hydrogenated over Raney nickel at room temperature and pressure : 1 mol. of hydrogen was taken up in about 40 hr. The catalyst was removed and the filtrate was acidified and concentrated *in vacuo* to give colourless plates of 5-*iso*propylhydantoin (1·35 g.), m. p. 145—146° alone or mixed with an authentic specimen (Gaudry, *Canad. J. Res.*, 1946, **24**, *B*, 301).

Reaction of Dimethylpyruvic Acid and Thiourea.—A mixture of dimethylpyruvic acid (Ramage and Simonsen, *J.*, 1935, 532) (3·25 g.) and thiourea (2·13 g.) was heated under reduced pressure (*ca.* 60 mm.) in an oil-bath at 120° for 3 hr. and then at 140° for 2 hr. The gummy mixture was warmed with acetone (30 ml.), and the insoluble white powder (0·62 g.) was collected and crystallised from alcohol to give needles of 5-*iso*propylidenehydantoin, m. p. and mixed m. p. 274° (decomp.) (Found : C, 51·5; H, 5·5; N, 19·8. Calc. for $C_6H_8O_2N_2$: C, 51·4; H, 5·7; N, 20·0%). The acetone solution was evaporated to a gum which on trituration with chloroform deposited 0·75 g. of unchanged thiourea. The chloroform solution was evaporated and the residual oil was triturated with sodium hydrogen carbonate solution, whereupon it crystallised. The neutral *product* (0·60 g.) separated from benzene as a white powder, m. p. 128—130° (Found : C, 52·0; H, 6·2; N, 15·3; S, 17·1. $C_9H_{12}ON_2S$ requires C, 52·2; H, 6·5; N, 15·2; S, 17·4%). The aqueous solution was acidified, whereupon a fawn solid (0·38 g.) slowly separated. This *acid*, which contained no sulphur, crystallised from alcohol in colourless rectangular prisms, m. p. 158—160° (slight decomp.) (Found: C, 52·1; H, 6·5; N, 11·0. $C_{11}H_{16}O_5N_2$ requires C, 51·6; H, 6·3; N, 10·9%).

Reactions of 5-Substituted Tetrahydro-2-thioglyoxaline-4-thiocarboxylic Acids with Acetic Acid.—A solution of tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-thiocarboxylic acid (1 g.) in acetic acid (10 ml.) was refluxed for 30 min. The yellow solution gave a crystalline product when cooled and a further crop was obtained by addition of water. The combined solids (0·30 g., 33%) crystallised from alcohol as rectangular lemon platelets of 4-*iso*propylidene-2-thio-5-thiazolidone, m. p. and mixed m. p. 213—214° (Found : N, 8·0; S, 36·8. Calc. for $C_6H_7ONS_2$: N, 8·1; S, 37·0%). In a similar manner tetrahydro-5 :5-pentamethylene-2-thioglyoxaline-4-thiocarboxylic acid afforded 4-*cyclo*hexylidene-2-thio-5-thiazolidone (28%), which separated from 2-ethoxyethanol in brilliant yellow rhombic plates, m. p. and mixed m. p. 229° (decomp.) (Found : N, 6·6. Calc. for $C_9H_{11}ONS_2$: N, 6·6%). 5-Ethyltetrahydro-5-methyl- and tetrahydro-5 : 5-tetramethylene-2-thioglyoxaline-4-thiocarboxylic acids likewise gave 4-*sec.*-butylidene- and 4-*cyclo*pentylidene-2-thio-5-thiazolidones respectively, identified by mixed m. p.

Reaction of Tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-thiocarboxylic Acid with Acetic Acid and Acetic Anhydride.—A solution of the thio-acid (12 g.) in acetic acid (80 ml.) and acetic anhydride (40 ml.) was refluxed for 30 min., during which a white solid separated. After cooling, the solid (1·97 g.) was collected. This *compound* (possibly XVII) was insoluble in most solvents, but dissolved in boiling dimethylformamide, from which it separated after addition

of alcohol as a powder, m. p. 340° (decomp.) (Found: C, 46·6; H, 5·6; N, 18·1; S, 20·5. $C_{18}H_{16}O_2N_4S_2$ requires C, 46·1; H, 5·2; N, 17·9; S, 20·5%). (When this substance was boiled with 48% hydrobromic acid for 2 hr. it gave tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-carboxylic acid in 55% yield.)

The original filtrate was diluted with an equal volume of water and after 3 days the cream-coloured solid was collected (1·58 g.) and crystallised from ethyl acetate as colourless crystals of an *acetyl derivative*, m. p. 183°, of the thio-acid (Found: C, 41·7; H, 5·1; N, 11·5; S, 27·2. $C_8H_{12}O_3N_2S_2$ requires C, 41·4; H, 5·2; N, 12·1; S, 27·6%). The compound dissolved in sodium hydrogen carbonate solution with effervescence. With 5N-hydrochloric acid (90 min.; reflux) it gave tetrahydro-5 : 5-dimethyl-2-thioglyoxaline-4-carboxylic acid (53%), whereas with saturated ethanolic hydrogen chloride (19 hr.; cold) the corresponding ester was obtained in 46% yield.

Hydrolysis of 5-Substituted 2-Thiothiazolidine-4-carboxyamides.—5-Ethyl-5-methyl-2-thiothiazolidine-4-carboxyamide (0·4 g.) was refluxed in 5N-hydrochloric acid (20 ml.) for 7 hr. The cooled solution was extracted with ether and the extracts, after being washed, were themselves extracted with sodium hydrogen carbonate solution. Acidification of the aqueous phase and extraction with ether afforded 5-ethyl-5-methyl-2-thiothiazolidine-4-carboxylic acid as a gum, which was characterised as the phenethylamine salt (0·37 g.), m. p. 182—183° (decomp.) alone or mixed with an authentic specimen (Doyle, Holland, Marflitt, Nayler, and O'Connor, *loc. cit.*). Hydrolysis of 5 : 5-tetramethylene-2-thiothiazolidine-4-carboxyamide (1 g.) with boiling 5N-hydrochloric acid (25 ml.) gave the carboxylic acid (0·58 g.), which crystallised from water in colourless plates, m. p. 167—168° alone or mixed with an authentic specimen (Cook and Pollock, *J.*, 1949, 3007) (Found: C, 44·3; H, 5·2; N, 6·4. Calc. for $C_8H_{11}O_2NS_2$: C, 44·2; H, 5·1; N, 6·5%). The 5 : 5-pentamethylene analogue similarly afforded 5 : 5-pentamethylene-2-thiothiazolidine-4-carboxylic acid (92%), colourless needles (from water), m. p. 202—204° alone or mixed with an authentic specimen (Billimoria, Cook, and Heilbron, *J.*, 1949, 1437) (Found: C, 46·3; H, 5·6; N, 6·5. Calc. for $C_9H_{13}O_2NS_2$: C, 46·7; H, 5·7; N, 6·1%).

Experiments with 5-Ethyltetrahydro-5-methyl-2-thioglyoxaline-4-thiocarboxylic Acid.—Repeated crystallisation of the low-melting mixture of isomers of the thio-acid (VIII; R = Me, R′ = Et) (Table 2) from methylene dichloride gave a very small recovery of the pure β-*isomer*, m. p. 155—156° (decomp.) (Found: C, 40·8; H, 6·0; N, 13·6; S, 30·9. $C_7H_{12}ON_2S_2$ requires C, 41·2; H, 5·9; N, 13·7; S, 31·4%). Absorption: $\lambda_{max.}$ 244 mμ, ε 17,350 in EtOH.

A solution of the mixed isomers (from 6 g. of 4-*sec.*-butylidene-2-thio-5-thiazolidone) in alcohol (15 ml.) was treated with 10% aqueous sodium hydroxide (30 ml.), set aside for 24 hr., and acidified with concentrated hydrochloric acid to precipitate the crude α-isomer of the acid (4·58 g.), m. p. 117—123° (decomp.). Crystallisation from ethanol gave white clumps of the pure α-*isomer*, m. p. 138° (decomp.) (Found: C, 41·3; H, 5·6; N, 13·8; S, 31·3%). Absorption: $\lambda_{max.}$ 244 mμ, ε 17,350 in EtOH. The m. p.s of the α- and the β-acid were depressed on admixture. The final purification of the α-acid could be accomplished with smaller loss by treating a solution of the material, m. p. 117—123° (decomp.), in a little chloroform with phenethylamine, whereupon the almost pure α-*isomer* of *phenethylamine 5-ethyltetrahydro-5-methyl-2-thioglyoxaline-4-thiolcarboxylate* separated in high yield, m. p. 163—164° (decomp)., unchanged on crystallisation from water (needles) (Found: C, 55·5; H, 7·0; N, 13·1; S, 20·0. $C_{14}H_{22}ON_2S_2$ requires C, 55·4; H, 7·1; N, 12·9; S, 19·7%). Treatment of the salt with dilute hydrochloric acid gave the pure α-acid, m. p. 138° (decomp.).

The thio-acid (α-isomer, 2 g.) and potassium hydroxide (0·7 g.) in water (20 ml.) were shaken with methyl sulphate (1·2 ml.). After 30 min., *methyl 5-ethyltetrahydro-5-methyl-2-thioglyoxaline-4-thiolcarboxylate* (1·15 g.) was collected and crystallised from ethyl acetate in colourless prisms, m. p. 145—147° (Found: C, 43·7; H, 6·7; S, 29·2. $C_8H_{14}ON_2S_2$ requires C, 44·0; H, 6·5; S, 29·4%).

The thio-acid (α-isomer; 1 g.) in methanol (25 ml.) was saturated with dry hydrogen chloride at 0°, and set aside for 24 hr. After removal of solvent *in vacuo*, the oily residue was washed with sodium hydrogen carbonate solution, dried, and rubbed with ether to induce crystallisation. The α-*isomer* of *methyl 5-ethyltetrahydro-5-methyl-2-thioglyoxaline-4-carboxylate* (0·5 g.) crystallised from water in colourless needles, m. p. 146—148° (Found: C, 47·7; H, 7·8; N, 14·2; S, 16·4. $C_8H_{14}O_2N_2S$ requires C, 47·5; H, 7·0; N, 13·9; S, 15·9%). The α-*isomer* of the corresponding ethyl ester, similarly prepared in 81% yield and crystallised from ethyl acetate, had m. p. 111—112° (Found: C, 50·2; H, 7·9; N, 13·4; S, 15·4. $C_9H_{16}O_2N_2S$ requires C, 50·0; H, 7·5; N, 13·0; S, 14·8%).

The thio-acid (mixed isomers; 10·45 g.) was treated with ethanolic hydrogen chloride as

above to give a crude product (7·23 g.), m. p. 104—105°, mixed m. p. with the α-ester 95—96°. Crystallisation from ethyl acetate gave the β-*isomer* of the ethyl ester (4·61 g.), m. p. 111—112°, mixed m. p. with the α-isomer 97—99° (Found: C, 50·1; H, 7·8; N, 13·3; S, 15·2%).

The above ethyl ester (α-isomer; 1·45 g.) in alcohol (7 ml.) was set aside with aqueous 5N-sodium hydroxide (7 ml.) for 48 hr. Alcohol was removed *in vacuo*, and the residue acidified with hydrochloric acid. On storage at 0° the α-*isomer* of 5-ethyltetrahydro-5-methyl-2-thioglyoxaline-4-carboxylic acid (0·67 g.) separated; it crystallised from water in colourless prisms, m. p. 197—198° (Found: C, 44·7; H, 6·2; N, 15·2. $C_7H_{12}O_2N_2S$ requires C, 44·7; H, 6·4; N, 14·9%). The β-*isomer* of the acid, similarly prepared from the β-ester, crystallised from water as the hemihydrate, m. p. 193—195° (Found: C, 42·4; H, 6·6; N, 14·0; S, 15·8. $C_7H_{12}O_2N_2S,0{\cdot}5H_2O$ requires C, 42·6; H, 6·6; N, 14·2; S, 16·3%). A mixture of the isomeric acids had m. p. 173—177°.

5-cyclo*Pentylidene*-2-*thiohydantoin*.—A mixture of 2-thiohydantoin (2 g.), *cyclo*pentanone (8 ml.), and piperidine (8 ml.) was refluxed for 90 min., cooled, and poured into an excess of dilute hydrochloric acid. The crude 5-cyclo*pentylidene*-2-*thiohydantoin* (2·3 g.) was collected and crystallised from 2-methoxyethanol (charcoal) in small yellow crystals, m. p. 319° (decomp.) (Found: C, 52·9; H, 5·5; N, 15·8. $C_8H_{10}ON_2S$ requires C, 52·7; H, 5·5; N, 15·4%).

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The Selective Elution of Metals Adsorbed on Cation-exchange Resins by Organic Solvents. Part I.

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The use of organic solvents in admixture with mineral acids for the selective elution of cations adsorbed on the ion-exchange resin Zeo Karb 225 is investigated. By suitable control of water and acid added to the solvent, selective elution is obtained by using either ketones or alcohols. A procedure for the complete separation of copper and nickel using acetone containing 4% (v/v) of hydrochloric acid (*d* 1·18) and 10% (v/v) of water as eluting agent is described.

In some cases a mixture of cations adsorbed on an ion-exchange resin can be selectively eluted by a procedure which utilises only the difference in affinity of the resin for each component of the mixture. More usually, however, an eluting agent capable of forming complexes with some or all of the adsorbed cations is used. The complexing agent is so chosen that the most strongly adsorbed metals are those which form the least stable complexes with the eluting agent. The differences in affinity are thus effectively enhanced and better separations result. Eluting agents of this type have usually been aqueous solutions to which complex-forming agents have been added, the best-known example being the use of buffered ammonium citrate solutions for the separation of the rare earths.

Burstall, Forrest, Kember, and Wells (*Ind. Eng. Chem.*, 1953, **45**, 1648) have shown that complex metal cyanides adsorbed on an anion exchanger can be effectively eluted with organic solvents containing mineral acids and that it is possible by suitable choice of solvent and mineral acid to obtain selective extraction of the metals. The present work explores further the possibility of using organic solvents containing mineral acids and water as complex-forming eluting agents for the separation of metals adsorbed on

cation-exchange resins. Eluting agents of this type have been used extensively in partition chromatography on cellulose. Separations by paper chromatography, however, suffered from a number of limitations. If the mixture of cations to be separated is in a large volume of dilute solution a preliminary concentration is necessary to enable the solution of the mixture to be applied to the cellulose in small volume. The separation is often sensitive to the presence of interfering anions and removal of these may be imperative. Use of cation-exchange resins as adsorbents overcomes these two difficulties but the subsequent selective elution of the metals with aqueous eluting agents is often difficult or impossible.

It was considered that organic solvents containing mineral acids might be effective eluting agents for the removal of cations from ion exchangers for the following reasons: (1) The presence of mineral acid in the solvent would bring about some dissociation of the resin–cation complexes depending upon their relative affinities for the resin. (2) The cations produced by the dissociation would form in some cases complexes with the solvent whose movement down the column would be dependent upon the stability of the complexes with respect to both water and acid. (3) Two metals both forming suitable solvent-soluble complexes might be separated by a partition mechanism. This assumes that, at equilibrium, the concentration of water in the resin phase is greater than in the external solvent solution. It has been stated (Davies and Thomas, *J.*, 1952, 1607) that if acetone containing 30% of water is equilibrated with a 10% divinylbenzene cross-linked polystyrene resin in the hydrogen form, then the liquid in the resin phase has the composition 72% water, 28% acetone, and the outer liquid 75% acetone, 25% water. A similar type of distribution might be expected to occur with the solvents employed in the present work using the resin Zeo Karb 225. The covalent metal complex with the solvent would then be in contact with a predominantly aqueous phase in the resin. In these circumstances part of the complex would be extracted into the aqueous phase in the resin, where it would undergo dissociation to give metal ions capable of ion exchange with the resin.

The present paper is confined almost exclusively to a study of the elution of nickel and copper adsorbed on Zeo Karb 225. These two metals were chosen for study because of the difference in their solubility in organic solvents containing hydrochloric acid and because of the ease with which either could be determined. In further papers the study will be extended to include the separation of other metals and the use of resins other than Zeo Karb 225.

Experimental

(Percentages of acid and water are in terms of v/v, and hydrochloric acid was of *d* 1·18 where no other concentration is specified.)

In preliminary experiments, a study was made of the elution of zinc, cobalt, manganese, and nickel adsorbed on Zeo Karb 225 with acetone containing hydrochloric acid, and the elution of various mixtures of iron, copper, cobalt, manganese, and nickel with ethyl methyl ketone containing hydrochloric acid. Both groups of metals are given in the order in which they were eluted, the first mentioned being the most easily eluted. In both cases the order of elution is the same as that obtained in cellulose chromatography (Burstall, Davies, Linstead, and Wells, *J.*, 1950, 516). In neither case was complete separation obtained, but results were sufficiently promising to encourage further experiments on simpler mixtures. Attention was therefore directed to the separation of nickel and copper and a study was made of the elution of these metals with acetone containing hydrochloric acid and with a number of alcohols containing hydrochloric acid.

The need for conditioning the column became apparent during the preliminary experiments using as solvent ethyl methyl ketone containing hydrochloric acid. While the water content of the solvent was closely controlled, less control had been kept on the water both inside and outside the resin beads before elution was carried out. The interstitial water could be replaced by eluting the resin with a small volume of solvent not containing acid before elution with the acid-bearing solvent. This solvent would also tend to displace water from the resin beads and could therefore be expected to have an effect on the separation. A number of experiments was carried out to ascertain the effect of various conditioning procedures. A series of four pairs of columns 1 cm. in diameter, each containing 5 g. of the resin Zeo Karb 225 in the hydrogen form,

was prepared. On to one of each pair were adsorbed 25 mg. of ferric ion and on to the other 25 mg. of cupric ion. Each column was then washed with 50 ml. of water and each pair of columns was subjected to different conditioning procedures. Through each column were passed 50 ml. of a conditioning solvent followed by 150 ml. of ethyl methyl ketone containing 9% of 1·5N-hydrochloric acid, this solvent giving normally a reasonable separation of iron from copper. The acid solvent eluate was collected in 50-ml. fractions and analysed (results in Table 1).

TABLE 1. *Conditioning of column.*

	Metal (%) eluted per 50-ml. fraction of COEtMe containing 9% of 1·5N-HCl							
	Copper fractions				Iron fractions			
Conditioning solvent	1	2	3	Total	1	2	3	Total
H_2O	0·17	0·28	0·36	0·81	83·6	14·0	1·2	98·8
COEtMe	33·2	0·38	0·13	33·7	93·5	2·6	2·8	98·3
COEtMe satd. with H_2O	0·12	0·09	0·05	0·26	66·5	29·2	1·1	96·8
COEtMe + 7·5% (v/v) H_2O	0·25	0·09	0·11	0·45	84·5	8·4	1·6	94·5

When the column was conditioned with dry ethyl methyl ketone the first fraction of eluting solvent contained a large amount of copper, but further fractions only small quantities. It appeared that the resin was first dehydrated by the passage of the dry ketone and that, when acid-bearing solvent was run down the column, water was extracted from the solvent by the resin. This resulted in the first part of the elution being carried out with a solvent of high acid but low water content which extracted copper. Once the resin attained equilibrium with the solvent the copper elution fell off rapidly. If the column was conditioned with water-saturated solvent, which in this case contained almost the same amount of water as the eluting solvent, only a small amount of copper was removed. Conditioning solvent containing slightly less water led to a small increase in the amount of copper eluted. Conditioning with water alone resulted in a steadily increasing quantity of copper appearing in the volume of solvent required for the elution of iron. In view of these results, in all further experiments the columns were conditioned by the passage of 25 ml. of the solvent identical with the eluting solvent except that the acid was replaced by an equal volume of water.

A standardised technique was developed for evaluating each solvent mixture. Columns about 15 cm. long and 1 cm. in diameter containing the equivalent of 5 g. of dry Zeo Karb 225 resin in the hydrogen form were used in all cases. The adsorption stage was carried out by passing through a column 50 ml. of a chloride solution of the metal under test containing about 8·5 mequiv. of the metal. The metal ion was adsorbed usually as a brightly coloured band on the top third of the column, which was then washed with 50 ml. of water. The column was treated with 25 ml. of conditioning solvent followed by 100 ml. of eluting solvent flowing at 50 ml. per hour. After elution the solvent was removed by evaporation and the metals determined. Copper was determined by electrolysis or colorimetrically with sodium diethyldithiocarbamate, and nickel by precipitation by dimethylglyoxime or colorimetrically with the same reagent. The columns were regenerated for re-use by elution with at least 200 ml. of 4N-hydrochloric acid and subsequently washing them with water until free from acid. The solvents were standardised by titration against N/10-sodium hydroxide. For the determination of trace quantities of nickel in eluates containing copper, a paper-chromatographic technique was used. The eluate was evaporated to dryness and the residue was redissolved in a small, measured volume of dilute hydrochloric acid. A 0·01-ml. aliquot part of the acid solution was applied to a strip of Whatman's No. 1 filter paper (CRL/1 pattern) and the chromatogram developed with acetone containing 5% of hydrochloric acid. The nickel was detected by spraying the strip with an alcoholic solution of rubeanic acid and estimated by comparison with a series of standard strips. It was possible to detect as little as 0·1 μg. of nickel in the presence of several mg. of copper.

Elution of Copper and Nickel with Acetone Solvents.—The first series of experiments were designed to determine the effect of variation in the hydrochloric acid and water content of the acetone eluting solvent on the extraction of copper and nickel. Aqueous solutions of nickel chloride containing approximately 5 g. of Ni/l. and of cupric chloride containing approximately 5·4 g. of Cu/l. were prepared. Portions of 50 ml. of these solutions contained approximately 8·5 mequiv. of the metal; thus the resin column was loaded to about one-third of its total capacity. This degree of loading was arbitrarily chosen. Later experiments on the effect

of loading indicated that a 25% loading was the maximum for optimum separations. The eluting solvent was prepared by mixing together measured volumes of acetone, hydrochloric acid, and water and ignoring changes in volume. The results of a series of experiments carried out with three eluting solvents containing different acid concentrations are shown in Fig. 1 and Table 2. (A dash in all tables of results indicates that no determination was carried out at this level.)

TABLE 2. *Elution of nickel and copper with acetone–HCl–H_2O mixtures.*

		Metal (%) eluted in 100 ml.						
		Water (%) added to eluting solvent						
HCl (%) in eluting solvent	Metal	0	5	10	25	50	75	No ketone
3	Ni	Nil	—	—	Nil	Nil	0·1	1·3
	Cu	89·0	96·5	92·0	0·1	Nil	0·2	0·4
4	Ni	0·2	0·1	Nil	Nil	Nil	0·4	6·8
	Cu	90·4	99·0	98·9	20·2	0·1	1·2	13·6
5	Ni	0·9	—	—	Nil	0·2	7·7	34·0
	Cu	95·1	—	96·4	28·8	6·2	19·0	35·0

When the eluting solution consisted largely of acetone and acid, little or no nickel was eluted, but the amount of copper eluted was at a considerably higher level. Furthermore, this amount of copper is higher than would normally be eluted with an aqueous solution containing the same proportion of acid. The small amount of nickel eluted when the solvent consisted solely of acetone and concentrated hydrochloric acid was largely held back by addition of a small amount of water (up to 10% v/v) to the solvent. Furthermore, when this was done the rate of copper elution increased slightly. The quantity of both nickel and copper eluted was very small when roughly equal proportions of acetone and water were present in the eluting solvent. The mechanism of the extraction was emphasised by the colour changes which occurred. On adsorption, copper formed a dark blue band and nickel a dark green band at the top of the column. On elution with an acid acetone solvent containing little water, copper was extracted and formed a characteristic orange-brown coloured complex in the ketonic solvent. When it was eluted with a solvent in which the acetone was partially replaced by water, the intensity of the orange colour tended to fade, until, on elution with aqueous hydrochloric acid, the eluted copper solution had the characteristic green colour of aqueous copper chloride solutions. No comparable colour changes occurred with the nickel which, when eluted at all, was obtained in a solution having the normal green colour of aqueous nickel chloride solutions.

(a) *Complete elution of copper.* The results in Fig. 1 and Table 2 were all based on collecting 100 ml. of eluting solution. From previous experience it would be necessary to use a considerably larger volume of solvent to remove the last traces of the mobile metal from the columns. Further experiments were therefore carried out on selected solvents to ascertain the volume of solvent necessary to obtain 100% extraction of copper.

Elution with acetone containing 2—3% of hydrochloric acid showed that 800 ml. were necessary to remove all the copper from the column. From a study of the curves in Fig. 1 it appeared that acetone containing 4% of HCl and 10% of H_2O might be a more efficient eluting

TABLE 3. *Elution of copper and nickel with acetone + 4% of* HCl *+ 10% of* H_2O.

Solvent fraction (each of 50 ml.)	Copper eluted *		Nickel eluted *		Solvent fraction (each of 50 ml.)	Copper eluted *		Nickel eluted *	
	Wt. (mg.)	%	Wt. (mg.)	%		Wt. (mg.)	%	Wt. (mg.)	%
1	163·1	61·09	0·004	0·002	5	0·092	0·035	0·065	0·027
2	98·6	36·93	0·005	0·002	6	0·021	0·008	0·124	0·051
3	5·1	1·91	0·009	0·004	7	0·031	0·012	0·28	0·116
4	0·165	0·062	0·023	0·009	8	0·016	0·006	0·46	0·19
						Total 100·05		Total 0·401	

* Solvents 0·494N (for Cu) and 0·488N (for Ni) with respect to acid.

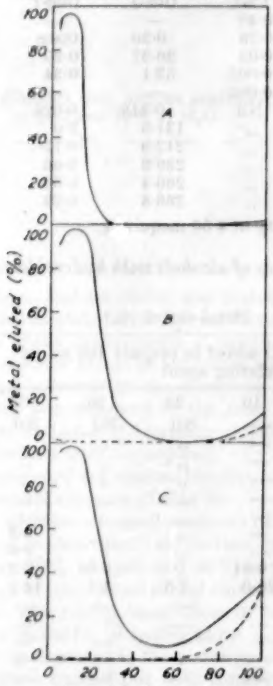
agent for copper, while at the same time nickel would remain adsorbed on the resin. Results obtained with this solvent are shown in Table 3 and indicate that only 400 ml. were required for complete elution of copper.

About 99·9% of the copper was extracted in the first 150 ml. of the solvent; the remainder trailed very badly. Under similar conditions a small amount of nickel was eluted. The amount of nickel was possibly dependent on the total loading of the column and further experiments

were carried out to ascertain the maximum loading at which a separation of copper and nickel adsorbed on the same column could be achieved.

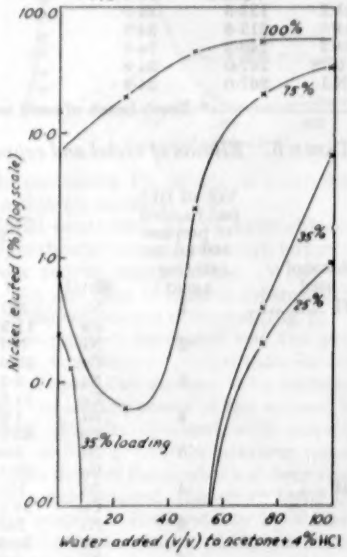
(b) *Effect of column loading on elution of nickel and copper.* In an initial experiment the capacity of the Zeo Karb 225 resin for nickel was found to be 4·82 mequiv./g. of dry resin. A series of experiments was then carried out in which 5-g. columns of resin were loaded to 25, 35, 50, 75, and 100% of their total capacity with nickel. The columns were eluted at each degree of loading with 100 ml. of acetone containing 4% of hydrochloric acid containing varying amounts of water. The results shown graphically in Fig. 2 indicate that the nickel eluted was negligible with a loading of 25% or less of the total capacity with the acetone containing 4% HCl

FIG. 1. *Elutions with acetone + HCl + H_2O.*



A, 3% HCl; *B*, 4% HCl; *C*, 5% HCl.
– – – Ni; —— Cu.

FIG. 2. *Effect of loading on elution.* (% refer to loading.)



solvent, providing the water added to the solvent was between 0 and 50%. In a check experiment in which 0·1938 g. of nickel was adsorbed on a 5-g. column of resin (equivalent to 27·4% loading) only 0·00001 g. of nickel was eluted with 400 ml. of acetone containing 4% of HCl and 10% of H_2O, and in a further similar experiment with a column loading of 25·1% no nickel was eluted with 400 ml. of solvent.

(c) *Separation of copper and nickel.* All elutions had so far been carried out with columns on which only one metal was adsorbed. Further experiments were carried out in which a mixture of nickel and copper was adsorbed on the resin. In all cases the total quantity of copper and nickel adsorbed on a column was equivalent to less than 35% of the total capacity of the resin and in all cases satisfactory recovery of copper was obtained by using 400 ml. of acetone containing 4% of hydrochloric acid and 10% of water (Table 4). When the amount of nickel present on the resin was greater than the amount of copper present, the separation was not quite complete if the total loading of the resin exceeded 25% of its capacity. When copper was in excess of nickel, a quantitative separation was achieved with resin loadings up to 35% of the total possible.

This was probably due to two causes: first, to the smaller quantity of nickel present, and secondly, to some reduction in the effective hydrochloric acid concentration in the solvent brought about by the use of hydrochloric acid to form the ketone-soluble copper chloride complex. The high copper figure obtained in the second experiment recorded in Table 4 was due to interference, by the trace of eluted nickel, in the colorimetric determination of the copper.

TABLE 4. *Separation of copper and nickel.*

			Nickel eluted			Copper eluted		
Ni on resin (mg.)	Cu on resin (mg.)	Total column loading (%)	In 1st 200 ml. (mg.)	In 2nd 200 ml. (mg.)	Total (%)	In 1st 200 ml. (mg.)	In 2nd 200 ml. (mg.)	Total (%)
242·3	Nil	34·3	0·04	0·93	0·40	—	—	—
242·3	0·245	34·3	0·06	0·62	0·28	0·30	trace	124·5
218·1	26·7	34·3	Nil	0·07	0·03	26·37	0·20	99·5
193·8	53·4	34·4	,,	0·01	0·005	53·1	0·34	100·1
193·8	Nil	27·4	,,	0·01	0·005	—	—	—
165·8	0·320	25·1 *	,,	Nil	Nil	0·318	0·026	107·5
121·2	133·5	34·5	,,	,,	,,	131·5	2·0	100·0
48·5	213·6	34·8	,,	,,	,,	212·9	0·17	99·8
24·2	240·3	34·8	,,	,,	,,	239·8	0·56	100·0
0·28	267·0	34·9	,,	,,	,,	266·4	0·60	100·0
Nil	267·0	34·9	,,	,,	,,	266·8	0·23	100·0

* Fresh batch of resin used with capacity of 4·50 mequiv./g.

TABLE 5. *Elution of nickel and copper with mixtures of alcohols with hydrochloric acid and water.*

			Metal eluted (%)						
			Vol. (ml.) of H_2O added to prepare 100 ml. of eluting agent						
Alcohol used	Vol. of HCl (ml.) added to prepare 100 ml. of eluting agent	Metal	0	5	10	25	50	75	No alcohol
MeOH	1	Ni	Nil	—	—	Nil	Nil	Nil	Nil
		Cu	11·5	—	—	,,	,,	,,	,,
	2	Ni	Nil	—	—	,,	,,	,,	,,
		Cu	58·6	—	—	,,	,,	,,	,,
	3	Ni	0·3	—	—	,,	,,	,,	1·3
		Cu	71·6	—	—	,,	,,	,,	0·4
	4	Ni	1·6	Nil	—	,,	,,	0·6	6·8
		Cu	82·9	40·0	—	,,	,,	0·6	13·6
	5	Ni	4·6	0·01	<0·01	,,	<0·01	6·3	29·2
		Cu	90·2	58·7	20·0	2·5	1·1	14·2	29·6
PrⁱOH	4	Ni	Nil	—	—	—	—	—	6·8
		Cu	18·9	—	—	—	—	—	13·6
	6	Ni	Nil	—	—	—	—	—	—
		Cu	34·6	—	—	—	—	—	—
	8	Ni	0·05	—	—	—	—	—	—
		Cu	48·1	—	—	—	—	—	—
	10	Ni	0·3	0·03	Nil	0·8	18·6	58·7	83·9
		Cu	52·2	66·9	69·4	47·3	55·3	81·7	90·2
PrⁿOH	10	Ni	1·8	—	—	—	—	—	83·9
		Cu	69·4	—	—	—	—	—	90·2
$C_5H_{11}OH$ ("AnalaR")	10	Ni	0·4	—	—	—	—	—	83·9
		Cu	85·5	—	—	—	—	—	90·2

(d) *Behaviour of other elements.* The behaviour of a number of other elements under the conditions used for the separation of copper and nickel was investigated. In each case 8·5 mequiv. of the metal in chloride solution were adsorbed on a 5-g. column of resin. The elution was carried out with 250 ml. of acetone containing 4% of HCl and 10% of H_2O. As is shown in Fig. 3, manganese was eluted very slowly and only 7% of the manganese present was removed with 250 ml. of solvent. Cobalt was eluted more rapidly but the total eluted was only 64%. The elution of iron was similar to that of copper initially but the tendency to trail was more marked; 99·6% of the iron was removed in 250 ml. of solvent.

Elution of Copper and Nickel with Alcohols.—The technique used was the same as that employed with the acetone solvent mixtures. It was noted in all experiments with alcohols that the eluted copper solution was a bright yellowish-green as opposed to the orange-brown solution obtained with ketones.

(a) *Elutions with methanol.* In a series of experiments a study was made of the effect of the concentration of hydrochloric acid and water added to the methanol. Results (Table 5) were similar to those obtained with acetone in that the rate of elution of copper and nickel increased as the acidity of the solvent increased but decreased sharply as water was added to the solvent. Unlike the results with acetone, no initial rise in the rate of elution of copper was obtained when up to 10% of water was added to the system. This tendency for the copper to be more efficiently eluted as the water concentration in the system was lowered, was further confirmed by an elution carried out with methanol containing dry hydrogen chloride in proportion equivalent to 2% of hydrochloric acid. This solvent eluted 71·7% of the copper compared with 58·6% eluted with methanol containing 2% of the acid. Results with the dry solvent for nickel elution

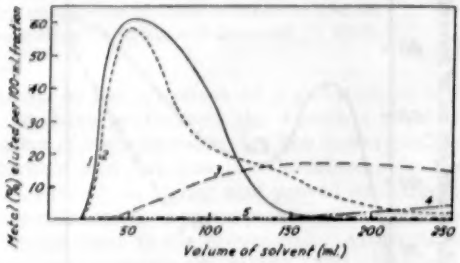


FIG. 3. *Elutions with acetone containing* 4% *of* HCl *and* 10% *of* H_2O.
—— Cu. – – – – Fe. — — Co. —·— Mn. —··— Ni.

were similar, and no nickel was eluted with methanol containing 1% or 2% of acid; 9·8% of the nickel was eluted with the methanol–dry hydrogen chloride mixture.

From these experiments it appeared that methanol containing 4% of hydrochloric acid and 5% of water would be a suitable solvent for the separation of copper and nickel, but attempts to use this solvent for the complete elution of copper proved impracticable. While 40% of the copper was removed in the first 100 ml. of solvent, the rate of elution subsequently fell off sharply and after the passage of 500 ml. only 75% of the copper was extracted (Fig. 5).

(b) *Elutions with* iso*propanol.* In elutions with *iso*propanol–hydrochloric acid the quantity of acid necessary for reasonable elution was, as expected, considerably greater than for acetone and methanol elutions (Table 5). *iso*Propanol behaved more like acetone than methanol in that the addition of small amounts of water increased the eluting power of the solvent, which subsequently decreased as further water was added. Results obtained with *iso*propanol containing 10% of acid and 10% of water are shown in Fig. 4. Unlike previous cases, the percentage of copper and nickel eluted in solvents in which most of the alcohol had been replaced by water, was higher than those in which the alcohol predominated, this effect being due to the larger quantity of hydrochloric acid present in the system. The tendency for the elution of copper to decrease as the water content of the solvent was reduced below 10% was confirmed by an elution carried out with *iso*propanol containing dry hydrogen equivalent to 10% of the acid, the elution of copper decreasing from 52·2% to 16·2%. In a similar experiment with nickel the quantity of eluted metal increased from 0·3% to 0·7%. It will be noted that the use of methanol or *iso*propanol containing dry hydrogen chloride led to an increase in the rate of elution of nickel. On the other hand, the rate of elution of copper was respectively increased and decreased with methanol and *iso*propanol each containing dry hydrogen chloride.

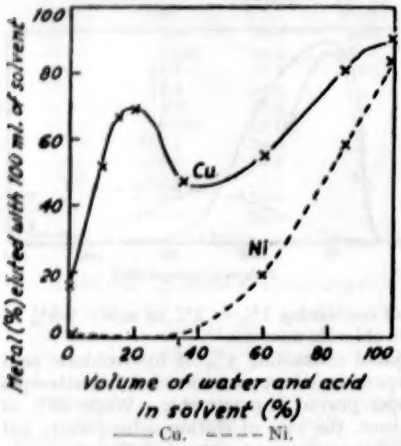
An attempt to use *iso*propanol containing 10% of acid and 10% of water for the complete elution of copper gave severe trailing, somewhat similar to that obtained when using methanol containing 4% of acid and 5% of water (Fig. 5). The total quantity of copper extracted was greater with the higher alcohol but trailing of the copper was sufficient to make use of this solvent impracticable.

(c) *Elutions with other alcohols.* Preliminary experiments were carried out on two other alcoholic solvents, *viz.*, *n*-propanol and pentyl alcohol, each containing 10% of acid. Results (included in Table 5) showed that the propanol solvent eluted copper more efficiently than did the *iso*propanol mixture containing the same amount of hydrochloric acid, but it also extracted a larger proportion of nickel. When compared with the *iso*propanol solvent, amyl alcohol containing 10% of acid eluted copper with a surprising efficiency, while causing only a small rise in the rate of nickel elution. This reversed the tendency shown with the lower alcohols for the rate of copper elution to decrease as the homologous series was ascended but this point

requires further investigation since the pentyl alcohol used was "AnalaR" containing a mixture of *iso*- and active pentyl alcohols.

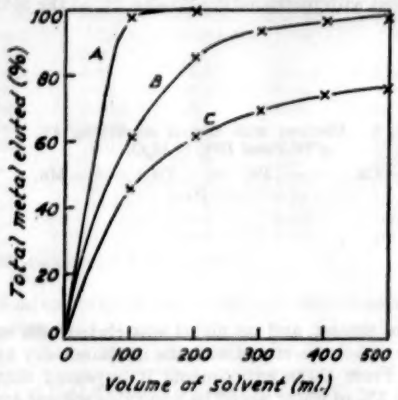
Discussion.—It has been shown that organic solvents containing water and mineral acid can be used for the selective elution of metals adsorbed on cation-exchange resins. Results obtained for the elution of copper and nickel adsorbed on the resin Zeo Karb 225 indicated that the use of acetone containing 4% of hydrochloric acid and 10% of water would provide the basis for an analytical separation of these metals. The large volume

FIG. 4. *Elutions with propan-2-ol containing 10% of HCl and 10% of H_2O.*



—— Cu. - - - - Ni.

FIG. 5. *Elution of copper with various solvents.*



A, Acetone containing 4% of HCl and 10% of H_2O.
B, Propan-2-ol ,, 10% ,, 10% ,,
C, Methanol ,, 4% ,, 5% ,,

of solvent (400 ml. for a 5-g. column) required for the complete elution of copper would be a disadvantage, and the cause, together with means of preventing this trailing elution of copper, requires further investigation. It is suggested that the use of other resins, particularly those with a lower degree of cross-linking, might result in a decrease in the consumption of solvent. Although only the elution of nickel and copper has been studied in detail, preliminary experiments with other metals indicate that by suitable choice of solvent and control of added water and acid other separations would be possible.

The effect of variation in the acid and water content of the eluting solvent on the removal of copper and nickel was, in general, as expected. An increase in acid concentration in the solvent led invariably to a more rapid elution of both metals. The sharp decrease in the eluting powers of both the ketones and alcohols studied, when their water content was raised to more than 20%, was in agreement with the known instability of the solvent-soluble complexes of these metals to water. As the water content of the solvent approached 100%, the eluting powers of the mixture began to increase again as a result of the increased polarity of the solvent mixture. A point of special interest was the temporary increase in the rate of copper elution with acetone containing hydrochloric acid when the amount of added water was increased from zero to about 5%. A similar effect obtained with *iso*propanol indicated that with these solvents some water was necessary for the formation of the solvent-soluble complex. This was further emphasised by the very sharp decrease in the elution of copper when a mixture of *iso*propanol with dry hydrogen chloride gas was used as eluting agent. A similar effect was not observed with methanol; this is possibly due to the higher polarity of the solvent, with the possibility of methanol replacing water in the solvent-soluble complex.

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The Synthesis of Methyl Ethers of Mannuronic and Glucuronic Acid, and their Reaction with Periodate.

By R. A. Edington, E. L. Hirst, and Elizabeth E. Percival.

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4-*O*-Methyl-D-mannuronic and 2 : 3-di-*O*-methyl-D-glucuronic acid have been synthesised for the first time and characterised by crystalline derivatives. 2 : 3 : 4-Tri-*O*-methyl-D-mannuronic acid has also been characterised as the crystalline methyl 2 : 3 : 4-tri-*O*-methyl-α-D-mannosiduronomethylamide. The action of periodate under varying conditions on these substances and on the two methyl ethers of D-galacturonic acid (Edington and Percival, *J.*, 1953, 2473) has been studied.

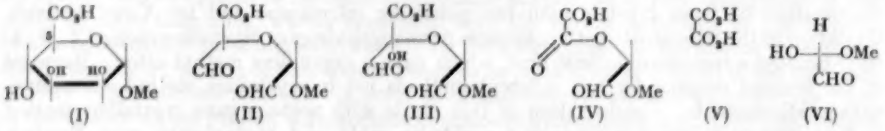
In continuation of our work on the synthesis of methyl ethers of D-galacturonic acid (Edington and Percival, *J.*, 1953, 2473) we have synthesised the 4-methyl ether of D-mannuronic acid and the 2 : 3-dimethyl ether of D-glucuronic acid. The first crystalline derivative of 2 : 3 : 4-tri-*O*-methyl-D-mannuronic acid has also been obtained. As the preparation of pure D-mannuronic acid derivatives from alginic acid proved exceedingly difficult it was considered preferable in the present work to prepare authentic crystalline derivatives of methyl α-D-mannoside and oxidise these to the uronic acid. Attempts to prepare crystalline methyl 2 : 3-*O*-*iso*propylidene-α-D-mannopyranoside (Ault, Haworth, and Hirst, *J.*, 1935, 517) and methyl 2 : 3-*O*-*iso*propylidene- and 2 : 3-*O*-benzylidene-6-*O*-toluene-*p*-sulphonyl-α-D-mannopyranoside were all unsuccessful. Accordingly crystalline methyl 2 : 3 : 4-*O*-tribenzoyl-6-*O*-toluene-*p*-sulphonyl-α-D-mannopyranoside (Haskins, Hann, and Hudson, *J. Amer. Chem. Soc.*, 1946, 68, 628) was utilised, and although the removal of the toluene-*p*-sulphonyl group by reduction (Kenner and Murray, *J.*, 1949, S178) could not be achieved this group was easily replaced by iodine; the latter was resistant to direct substitution by the hydroxyl group, but was easily replaced by nitrate. Reductive denitration then gave crystalline methyl 2 : 3 : 4-tri-*O*-benzoyl-α-D-mannoside. Parallel experiments on the successive treatment with triphenylmethyl chloride and benzoyl chloride of methyl α-D-mannopyranoside in pyridine gave methyl 2 : 3 : 4-tri-*O*-benzoyl-6-*O*-triphenylmethyl-α-D-mannoside and this with hydrogen bromide in glacial acetic acid gave the same crystalline tribenzoate in high yield. As originally obtained or after recrystallisation from aqueous pyridine, methyl 2 : 3 : 4-tri-*O*-benzoyl-6-*O*-triphenylmethyl-α-D-mannoside contained one molecule of firmly held pyridine of crystallisation and analogous compounds containing chloroform or acetone of crystallisation were obtained by recrystallisation from the corresponding solvent. The pyridine of crystallisation did not interfere with the removal of the trityl residue. Dr. C. A. Beevers kindly undertook an examination of these crystals with the polarising microscope and by *X*-ray analysis. Oxidation of the tribenzoate with potassium permanganate gave crystalline methyl 2 : 3 : 4-tri-*O*-benzoyl-α-D-mannosiduronic acid, which gave a crystalline methyl ester. Removal of the benzoyl residues by two different methods led to crystalline methyl α-D-mannopyranosiduronamide. Condensation of this amide with acetone gave crystalline methyl 2 : 3-*O*-*iso*propylidene-α-D-mannopyranosiduronamide and methylation with Purdie's reagents gave a crystalline product which was analysed as methyl 4-*O*-methyl-2 : 3-*O*-*iso*propylidene-α-D-mannosiduronomethylamide. The fact that the amide group had also been methylated was confirmed by conversion into the methyl ester and regeneration of the original substance by treatment with methylamine. This was further characterised by acid hydrolysis, followed by bromine oxidation and the isolation, as its crystalline diamide, of 4-*O*-methyl-D-mannaric acid (equivalent, by reason of the symmetry, to 3-*O*-methyl-D-mannaric acid).

Although 2 : 3 : 4-tri-*O*-methyl-D-mannuronic acid has been synthesised previously (Smith, Stacey, and Wilson, *J.*, 1944, 131; Ault, Haworth, and Hirst, *loc. cit.*) no crystalline derivative except the trimethylmannaramide was isolated. In the present work methylation with Purdie's reagents of methyl α-D-mannopyranosiduronamide gave crystalline

methyl 2 : 3 : 4-tri-*O*-methyl-α-D-mannosiduronomethylamide. Again proof that the amide group had been methylated was obtained by hydrolysis and regeneration by treatment with methylamine. The regenerated material was further characterised, after hydrolysis and oxidation, as crystalline 2 : 3 : 4-tri-*O*-methyl-D-mannardiamide.

Although 2 : 3-di-*O*-methyl-D-glucuronic acid was isolated by Smith (*J.*, 1940, 1035) from methylated arabic acid no authentic synthesis of it has been reported. Methylation of methyl 4 : 6-*O*-benzylidene-α-D-glucoside (Freudenberg, Toepffer, and Andersen, *Ber.*, 1928, **61**, 1750) gave the crystalline 4 : 6-*O*-benzylidene-2 : 3-di-*O*-methyl derivative from which the benzylidene residue was removed by dilute acid at room temperature. Oxidation of the crystalline product with dilute aqueous alkaline permanganate, followed by esterification, led to syrupy methyl (methyl 2 : 3-di-*O*-methyl-α-D-glucopyranosid)uronate, which gave a crystalline *p*-nitrobenzoate identical (mixed m. p.) with a specimen prepared by Smith (*loc. cit.*) from the hydrolysate of methylated arabic acid. The crystalline phenylhydrazide of the 2 : 3-dimethyl ether was also prepared and had m. p. 195—197°. Smith (*loc. cit.*) records m. p. 225—227° for this derivative and we are grateful to him for a re-determination : his material had changed on storage to m. p. 207° (205° after resolidifying) and gave a mixed m. p. with our material of 196—200° (197° after resolidifying). The existence of two crystalline forms is not new in carbohydrate chemistry (cf. 2 : 3-di-*O*-methyl-*N*-phenyl-D-xylosamine, m. p. 144° and 126°; Smith *et al.*, *J. Amer. Chem. Soc.*, 1952, **74**, 1341). The dimethyl ether was further characterised by conversion into the known methyl 2 : 3 : 4-tri-*O*-methyl-α-D-glucosiduronamide and 2 : 3-di-*O*-methyl-D-glucaramide.

In spite of the fact that the original concept of specificity for the α-diol structure has been modified considerably, periodate remains a valuable tool. The presence of uronic acid residues in many polysaccharides makes it desirable, therefore, that precise information should be available concerning the reaction of these substances and their derivatives with periodate. Link and his co-workers (*J. Biol. Chem.*, 1945, **159**, 502) recorded that zinc bornyl glucosiduronate and methyl (methyl α-D-galactosid)uronate gave more than the theoretical amount of formic acid under the action of periodate. Halsall, Hirst, and Jones (*J.*, 1947, 1427) confirmed this and found that if they used potassium metaperiodate at pH 4 and kept the concentration of formic acid low the uronic acids underwent further oxidation. Link and his colleagues had explained the over-oxidation of the uronosides on the assumption that after the formation of the dialdehyde (II) the hydrogen situated on the original $C_{(5)}$ is activated by the adjacent carboxyl and aldehydic groups and is oxidised to a hydroxyl group (as in III). " This would result in the formation of a substance which in its hydrated form contains hydroxyl groups on adjacent carbon atoms and would undergo further oxidation with periodate with the formation of an ester of oxalic acid " (IV). At this stage the consumption of periodate is 4 mol. per mol. of uronic



acid. If the conditions are such that the ester (IV) is hydrolysed, the hemiacetal (VI) of glyoxal would be oxidised further and the total consumption of periodate would be 5 mol. Sprinson and Chargaff (*J. Biol. Chem.*, 1946, **164**, 435) investigated the conversion of the aldehyde (II) into the hydroxy-aldehyde (III) and proved that substances such as malonic acid which contain a hydrogen atom on a carbon atom situated between two carbonyl groups can be oxidised to the corresponding hydroxy-compound which then undergoes further oxidation.

In the present work methyl (methyl α-D-galactopyranosid)uronate was oxidised under different conditions of pH and temperature (see Table 1). Within 20 hours under all the conditions employed more than the 2 mol. of periodate required by the simple oxidation had been consumed. In 66 hours the consumption in all cases was 3 mol. or more and the

TABLE 1. *Uptake of periodate (mol.) by methyl α-D-galactopyranosiduronic methyl ester.*

Temp. :	18°						0°		
Buffer :	None	A	B	C	D	E	None	B	E
pH :	—	2·0	4·5	5·3	5·3	7·0	—	4·5	7·0
Time (hr.)									
20	3·5	2·9	2·9	3·0	3·1	4·2	2·5	2·4	3·1
66	4·0	3·2	3·2	3·8	4·7	4·9	3·0	3·0	4·7
140	4·7	3·5	3·3	4·9	5·0	5·0	3·1	3·0	4·9
300	5·1	3·8	4·1	5·1	5·1	5·1	4·0	4·0	5·0

reaction generally appeared to become slower after this point. In 300 hours reaction appeared to be complete at a consumption of 5·0—5·1 mol. except in four cases, notably at pH 4·5 at 0° and 18°, in which the consumption was still only 4·0—4·1 mol. Meyer and Rathgeb (*Helv. Chim. Acta*, 1949, **32**, 1102) state that, if the oxidation is carried out at 0° and the pH kept between 5·7 and 4·2, then the hydrolysis of formyl esters is negligible. It appears probable therefore that the oxidations carried out at pH 4·5 are arrested at the ester (IV). From the results it appears that some overoxidation occurs under all the conditions studied and that, apart from the figure of 5 mol. representing complete overoxidation, the only significant arrest in the progress of oxidation occurs at the α-hydroxy-aldehyde (III) after the consumptiom of 3·0 mol. of oxidant. According to Halsall, Hirst, and Jones (*loc. cit.*) this is to be expected as the rate of oxidation of the α-hydroxy-aldehyde is comparatively slow.

Of the four glycosiduronic acid derivatives studied (see Table 2) in which overoxidation

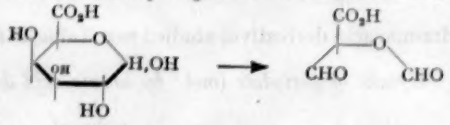
TABLE 2. *Uptake of periodate (mol.) by uronic acid derivatives.*

	Mol. expected			Buffer B pH 4·5, 0°		Buffer E pH 7·0, 18°	
Substance	(*a*)	(*b*)		90 hr.	300 hr.	90 hr.	300 hr.
Me (Me α-D-galactopyranosid)uronate	2	5		3·0	4·0	5·0	5·1
Me α-D-galactopyranosiduronamide	2	5		2·3	2·5	2·8	4·7
Me α-D-mannopyranosiduronamide	2	5		2·3	2·7	2·8	4·7
Me (Me 2-*O*-methyl-α-D-galactosid)uronate	1	3		1·4	2·0	2·0	3·0
Me (Me 4-*O*-methyl-α-D-mannosid)uronate	1	1		0·9	1·0	1·0	1·1
Me (Me 3 : 4-di-*O*-methyl-α-D-galactosid)uronate	0	0		0·0	0·0	0·0	0·0
Me (Me 2 : 3-di-*O*-methyl-α-D-glucosid)uronate	0	0		0·0	0·0	0·0	0·0
Me (Me 2 : 3 : 4-tri-*O*-methyl-α-D-glucosid)uronate	0	0		0·0	0·0	0·0	0·0
Me 2 : 3 : 6-tri-*O*-methyl-α-D-mannosiduronomethylamide	0	0		0·0	0·0	0·0	0·0
	(*c*)	(*d*)	(*e*)				
D-Galacturonic acid	5	3	5	3·3	3·6	—	—
D-Mannuronic acid	5	3	5	3·9	4·2	—	—
4-*O*-Methyl-D-mannuronic acid	3	2	2	2·0	2·1	—	—
2-*O*-Methyl-D-galacturonic acid	3	1	3	1·5	1·9	—	—
3 : 4-Di-*O*-methyl-D-galacturonic acid	2	1	1	1·1	1·2	—	—
2 : 3-Di-*O*-methyl-D-glucuronic acid	2	0	0	0·9	1·2	—	—
2 : 3 : 4-Tri-*O*-methyl-D-glucuronic acid	1	0	0	0·0	0·0	—	—

(*a*) Without overoxidation. (*b*) With overoxidation. (*c*) Open-chain configuration. (*d*) Pyranose, without overoxidation. (*e*) Pyranose, with overoxidation.

was expected it did occur, but the numerical results are difficult to reconcile with theory. At 0° and pH 4·5 the overoxidation was small even after 300 hours, methyl α-D-galacto-siduronamide and mannosiduronamide consuming respectively 2·5 and 2·7 mol. of periodate instead of the postulated 5 mol. Methyl (methyl 2-*O*-methyl-α-D-galactosid)uronate consumed 2 mol., mid-way between normal oxidation and complete overoxidation. No over-oxidation occurred with methyl (methyl 4-*O*-methyl-α-D-mannosid)uronate; on the current theories this is to be expected as the 4-methyl group would prevent oxidation between positions 3 and 4 and consequently the formation of an active hydrogen atom. This is also in agreement with the results of Smith (*J.*, 1951, 2646) who found that methyl (methyl 4-*O*-methyl-α-D-glucosid)uronate consumed only 1 mol. of periodate. With two dimethyl- and two trimethyl-uronosidic methyl esters where no oxidation of any kind was expected the results fitted expectations.

A number of free uronic acids were oxidised at 0° and pH 4·5 (see Table 2); under these conditions, if a formic ester is produced, it is unlikely to be hydrolysed (Meyer and Rathgeb, *loc. cit.*). The periodate consumption after 300 hours was in every case about 1 mol. less than would be expected if the uronic acid reacted in the straight-chain (aldehydo-)form. In every experiment the glycosiduronic ester was hydrolysed with N-sulphuric acid at 100° for 24 hours and no attempt was made to isolate the product before oxidation with periodate and it might be argued that low consumption of periodate was due to loss of sugar during hydrolysis. However, hydrolysis of methyl (methyl 3 : 4-di-*O*-methyl-α-D-galactosid)-uronic under the same conditions gave a 97% yield of the free acid. White (*J. Amer. Chem. Soc.*, 1953, **75**, 4692) found that 3 : 4-di-*O*-methyl-D-glucuronic acid consumed only 1 mol. of periodate which is in agreement with the present results for 3 : 4-di-*O*-methyl-D-galacturonic acid. Greville and Northcote (*J.*, 1952, 1945) found that 3 : 4-di-*O*-methyl-D-glucose consumed only 1 instead of 2 mol. of periodate which could be explained by assuming that the sugar reacts in the pyranose configuration, although these authors consider that the immunity of $C_{(3)}$ and $C_{(6)}$ to oxidation may only partly be due to the impossibility of the sugar's assuming the furanose configuration. Application of this concept to the uronic acids oxidised in the present work gives figures which fit experimental results in the case of 4-*O*-methyl-D-mannuronic acid, 3 : 4-di-*O*-methyl-D-galacturonic acid, and 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid. For the remaining uronic acids it must be borne in mind that if a uronic acid having 3- and 4-hydroxyl groups reacts in the pyranose form one of the intermediates contains activated hydrogen and overoxidation is therefore to be expected.



This overoxidation would be expected with D-galacturonic, D-mannuronic, and 2-*O*-methyl-D-galacturonic acid, in all of which the actual periodate consumption exceeds the figure predicted on the basis of pyranose configuration without overoxidation. 2 : 3-Di-*O*-methyl-D-glucuronic acid also consumes more periodate than would be expected from the pyranose form although in this case overoxidation due to activated hydrogen is hardly to be expected.

Experimental

All solvents were removed under reduced pressure and below 50°. M. p.s were determined on the Kofler hot-stage microscope. Silver and barium salts were removed by filtration through layers of charcoal and Celite and the residue on the filter washed at least thrice with a suitable warm solvent. Optical rotations were determined at 18° ± 2° in $CHCl_3$ unless otherwise stated. Light petroleum was the fraction of b. p. 60—80°.

Methyl 2 : 3 : 4-*Tri*-O-*benzoyl*-6-O-*triphenylmethyl*-α-D-*mannoside*.—Methyl α-D-mannopyranoside, m. p. 194—195° (105·5 g.), isolated from carob gum (supplied by Messrs. Ellis Jones, Stockport) (Smith, *J.*, 1948, 1989) was heated with triphenylmethyl chloride (175 g.) and dry pyridine (1050 ml.) at 50° with occasional shaking, until all the solid had dissolved (6 hr.), then kept at room temperature for 18 hr., after which benzoyl chloride (230 ml.) was added rapidly without cooling. The mixture was set aside at room temperature for 24 hr. and the crystalline solid filtered off, and washed with pyridine (100 ml.), with ethanol (2 × 100 ml.), with water (3 l.), and again with ethanol (2 × 100 ml.). After drying, the *product* was a colourless crystalline solid (368 g., 82%), m. p. 100—120°, $[\alpha]_D$ −110° (Found: C, 75·1; H, 5·3; N, 1·9. $C_{47}H_{40}O_9,C_5H_5N$ requires C, 75·4; H, 5·5; N, 1·7%). Recrystallisation from aqueous or ethanolic pyridine gave an unchanged product. Recrystallisation from acetone gave stout prisms, m. p. 100—115°, $[\alpha]_D$ −114° (Found: C, 74·2; H, 6·1. $C_{47}H_{40}O_9,C_3H_6O$ requires C, 74·3; H, 5·7%). Recrystallisation from ethanol–chloroform gave plates, m. p. 100—115°, $[\alpha]_D$ −107° (Found: C, 67·9; H, 5·0; Cl, 9·3; loss of wt. at 100°/15 mm. in 15 hr., 10·4. $4C_{47}H_{40}O_9,3CHCl_3$ requires C, 68·4; H, 4·9; Cl, 9·5; $CHCl_3$, 10·7%). The crystals from each of these solvents, after melting, recrystallised between 115—125° and had a final m. p. 188—189°. After removal of the solvent *in vacuo* the *product* was a fine white powder, m. p. 189—191°, $[\alpha]_D$ −121° (Found: C, 75·4; H, 5·3. $C_{47}H_{40}O_9$ requires C, 75·4; H, 5·4%).

Examination with the polarising microscope [Dr. Beevers]. Crystals from $CHCl_3$: flat

prisms showing an extinction at 45° to their length. Crystals from acetone: prisms, some with parallel and some with a 45° extinction. Crystals from aqueous pyridine: small prisms, a woolly mass, 22° extinction. Crystals from $CHCl_3$–EtOH: opaque mass, no single crystals visible. Conclusion: These crystals are of low symmetry, and perhaps show more than one crystal form.

X-Ray Examination [Dr. BEEVERS]. Oscillation and Weissenberg photographs (zero and first layer-line) were taken of two crystals from chloroform. Both specimens showed a similar phenomenon, a doubling of the spots, more pronounced in some directions than in others, indicating a twinning of two slightly different lattices very similar to one another. A detailed analysis of the two lattices has not been made, although it is thought that both are either monoclinic or triclinic. If the doubled spots are treated as one, an "average" lattice can be deduced, and has the following properties: monoclinic, $a = 9{\cdot}07$, $b = 24{\cdot}3$, $c = 10{\cdot}4$ Å, $\beta = 105°\ 27'$. This cell is body-centred (though of course it can be transformed into an A or a C face-centred lattice). The volume of the cell is 2209 Å^3, and this value gives 2·05 of (molecule + $\frac{1}{4}CHCl_3$) per cell. Since this refers to an "average" cell it is quite possible that there are 2 molecules of chloroform in one kind of cell and 1 in the other, although it might also be that there are 1·5 molecules in both kinds of cell. The two cells appear to be equally numerous, *i.e.*, the average intensity of the two sets of spots is about the same.

It is hoped that an opportunity may arise for the lengthy detailed study of these twins, especially as a large single crystal of the product from acetone is available.

Methyl 2:3:4-Tri-O-benzoyl-6-O-toluene-p-sulphonyl-α-D-mannoside.—Methyl α-D-mannoside (107 g.) was stirred with dry pyridine (1000 ml.) for 30 min. at room temperature, then cooled to 0°, and a solution of toluene-*p*-sulphonyl chloride (112 g., 1·05 equiv.) in pyridine (250 ml.) was added with stirring and cooling to 0° during 9 hr. After a further hour's stirring at room temperature the mixture was cooled to 0° and water (1000 ml.) added with vigorous stirring during 20 min. More water (1500 ml.) was added and the solution extracted with chloroform (4 × 600 ml.). The extracts were washed with water and dried. Removal of the solvent gave a yellow syrup (146 g., 76%) (Found: S, 9·2; $C_7H_7O_3SNa$, 54·3. $C_{14}H_{21}O_8S$ requires S, 9·2; $C_7H_7O_3SNa$, 55·8%). The syrup (146 g.) in pyridine (400 ml.) was treated with benzoyl chloride (258 ml., 4 equiv.) and set aside at room temperature for 24 hr. After treatment with water (20 ml.) the mixture was poured into saturated aqueous sodium hydrogen carbonate, a red gum separating. Repeated extraction under reflux with ethanol left a white residue of tribenzoate which recrystallised from chloroform–ethanol as colourless plates (157 g., 50% from methyl α-D-mannoside), m. p. 198°, $[\alpha]_D$ −104° (Haskins, Hann, and Hudson, *loc. cit.*, record 38% yield and m. p. 197—199°, $[\alpha]_D$ −102°) (Found: C, 63·5; H, 4·9; S, 5·1. Calc. for $C_{35}H_{32}O_{11}S$: C, 63·6; H, 4·9; S, 4·9%).

Methyl 2:3:4-Tri-O-benzoyl-α-D-mannoside.—(*a*) Methyl 2:3:4-tri-*O*-benzoyl-6-*O*-triphenylmethyl-α-D-mannoside (20 g.) was shaken vigorously for 90 sec. with hydrogen bromide (10%; w/v) in glacial acetic acid (33 ml.) and filtered immediately into a mixture of water (1500 ml.) and chloroform (1000 ml.). Fourteen further portions (each 20 g.) were treated in the same way and all were filtered into the same chloroform–water mixture. The aqueous layer was extracted with chloroform (2 × 400 ml.) and the combined chloroform extracts, after being washed and dried, gave a crystalline solid on evaporation. When an ethanol solution of this solid was kept overnight at room temperature crystalline starting material (5 g.; m. p. 95—120°, 187—189°) was deposited. Evaporation of the mother-liquors gave a crystalline *tribenzoylmannoside* (172 g., 95%), which after recrystallisation from aqueous alcohol had m. p. 143—145°, $[\alpha]_D$ −160° (Found: C, 66·6; H, 5·3. $C_{34}H_{28}O_9$ requires C, 66·4; H, 5·2%).

(*b*) The foregoing toluene-*p*-sulphonate was recovered unchanged and in good yield after hydrogenation with Raney nickel in ethyl acetate at 1 and 3 atm. during 72 hr. with shaking at 20°, at 100 atm. during 12 hr. with stirring, and under the conditions recorded by Mozingo *et al.* (*J. Amer. Chem. Soc.*, 1945, **67**, 2092) for 6 hr. at 77° with or without a stream of hydrogen. In a final experiment at 100°/100 atm. for 12 hr. a non-reducing syrup, $[\alpha]_D$ ±0°, was isolated (Found: C, 63·0; H, 7·4; S, 2·4; OMe, 6·7%; equiv., 184). It gave a negative test for primary toluene-*p*-sulphonyl ester (Tipson, Clapp, and Cretcher, *J. Org. Chem.*, 1947, **12**, 133).

(*c*) The toluene-*p*-sulphonate (6 g.) was converted into the 6-deoxy-6-iodo-derivative according to Oldham and Rutherford's method (*J. Amer. Chem. Soc.*, 1932, **54**, 366). Recrystallisation from acetone gave large prisms of the 6-iodide (5·05 g., 90%), m. p. 199—201°, $[\alpha]_D$ −106° (Found: C, 55·1; H, 4·1; I, 20·6. Calc. for $C_{28}H_{25}O_8I$: C, 54·5; H, 4·1; I, 20·6%). Treatment of this in dry benzene with dry or with moist silver oxide with vigorous shaking for 7 days, followed by filtration and evaporation, gave the starting material in quantitative yield. Heating

with moist silver oxide in benzene in a sealed tube at 100° for 2 hr. gave, after filtration and evaporation, a dark, reducing syrup.

The iodide (13 g.), in acetonitrile (200 ml.), was heated under reflux for 4 hr. with powdered silver nitrate (4 g.). Excess of silver nitrate was removed by treating the cooled solution with sodium iodide (1·0 g.) in acetone. After removal of the precipitated silver iodide the solution was diluted with chloroform (300 ml.) and extracted with water (3 × 300 ml.). Evaporation of the dried chloroform layer gave crystals from which unchanged starting material (6·2 g.; m. p. 193°) was removed by fractional crystallisation from ethanol. The more soluble *nitrate* was obtained from 90% ethanol as large prisms (5·5 g., 91%), m. p. and mixed m. p. with a specimen provided by Dr. G. O. Aspinall (prepared by direct nitration of methyl 2 : 3 : 4-tri-*O*-benzoyl-α-D-mannoside, unpublished work) 103—104°, $[\alpha]_D$ −116° (Found: C, 61·1; H, 4·5; N, 2·5. $C_{28}H_{25}O_{11}N$ requires C, 61·0; H, 4·6; N, 2·5%). A solution of this nitrate (2·0 g.) in glacial acetic acid (10 ml.) and benzene (20 ml.) was treated at room temperature with equal quantities of zinc and iron powders until the solution no longer gave a pink colour with diphenylbenzidine in concentrated sulphuric acid. Filtration and extraction with benzene, followed by aqueous washing of the benzene extracts and evaporation, gave crystals (1·3 g., 71%), m. p. 143° alone or mixed with the previous end-product (after recrystallisation from ethanol).

Methyl α-D-*Mannopyranosiduronamide*.—A solution of methyl 2 : 3 : 4-tri-*O*-benzoyl-α-D-mannoside (150 g.) in acetone (1500 ml.), glacial acetic acid (1500 ml.), and water (150 ml.) was stirred at room temperature, and potassium permanganate (160 g.; "AnalaR") was added in small portions during 30 hr. (Stacey, *J.*, 1939, 1529). After a further 18 hr. the solution was decolorised by aqueous potassium metabisulphite. 4N-Sulphuric acid (150 ml.) was added, and chloroform extraction (3 × 1000 ml.) followed by evaporation gave *methyl* 2 : 3 : 4-*tri*-O-*benzoyl*-α-D-*mannosiduronic acid* (131 g., 85%) which crystallised on storage and after recrystallisation from chloroform–light petroleum had m. p. 180—181·5°, $[\alpha]_D$ −140° (Found: C, 64·5; H, 4·7. $C_{35}H_{24}O_{10}$ requires C, 64·6; H, 4·6%). Treatment with methanolic hydrogen chloride (0·5%) at 20° for 72 hr. led to crystalline methyl (methyl 2 : 3 : 4-tri-*O*-benzoyl-α-D-mannosid)-uronate (123 g., 92%) which after recrystallisation from methanol had m. p. 143—144°, $[\alpha]_D$ −127° (Found: C, 65·2; H, 4·9. $C_{29}H_{26}O_{10}$ requires C, 65·1; H, 4·9%). This ester (100 g.) was dissolved in saturated methanolic ammonia (1100 ml.) and set aside at room temperature for 24 hr. Evaporation gave a syrup from which benzamide was removed by repeated extraction with ether (250-ml. portions). The crystalline residue of *methyl* α-D-*mannopyranosiduronamide* was washed once with acetone and recrystallised from aqueous acetone as colourless prisms (20·1 g., 52%), m. p. 182—183°, $[\alpha]_D^{18}$ +66° (*c*, 1·1 in H_2O) (Found: C, 41·0; H, 6·3; N, 6·6. $C_7H_{13}O_6N$ requires C, 40·6; H, 6·3; N, 6·7%). Removal of the benzoyl groups from the previous tribenzoate with sodium methoxide (Zemplén and Pacsu, *Ber.*, 1929, **62**, 1613), followed by esterification with methanolic hydrogen chloride (2%), gave syrupy methyl (methyl α-D-mannopyranosid)uronate, n_D^{19} 1·4842, $[\alpha]_D^{22}$ +80° (*c*, 0·5 in H_2O); the derived amide (45% yield from the tribenzoate ester) had m. p. and mixed m. p. 182—183°, $[\alpha]_D^{15}$ +63° (*c*, 0·9 in H_2O).

Methyl (*Methyl* 4-O-*Methyl*-α-D-*mannosid*)*uronate*.—The foregoing amide (20 g.) was condensed with acetone (750 ml.) (Percival and Percival, *J.*, 1950, 690). After 4 days the supernatant liquid was decanted off and neutralised with barium carbonate, and the residual solids were shaken for a further 2 days with acetone (500 ml.) containing sulphuric acid (0·03% v/v). Condensation of the residual solids with acetone was repeated a further 6 times after which the barium salts were removed from the combined neutral extracts. Evaporation of the acetone gave crystalline *methyl* 2 : 3-O-iso*propylidene*-α-D-*mannosiduronamide*, which recrystallised from acetone–light petroleum as large colourless prisms (15·0 g., 63%), m. p. 177·5—179°, $[\alpha]_D$ +14° (*c*, 1·0 in H_2O) (Found: C, 49·0; H, 6·8; N, 5·1. $C_{10}H_{17}O_6N$ requires C, 48·5; H, 6·9; N, 5·7%). Threefold methylation with methyl iodide and silver oxide gave *methyl* 4-O-*methyl*-2 : 3-O-iso*propylidene*-α-D-*mannosiduronomethylamide* (1·09 g. from 1 g.; 93%) which crystallised and after recrystallisation from light petroleum had m. p. 151—153°, $[\alpha]_D^{18}$ +23° (*c*, 0·6 in H_2O) (Found: C, 52·4; H, 7·7; N, 5·3. $C_{12}H_{21}O_6N$ requires C, 52·4; H, 7·6; N, 5·1%). Hydrolysis with 2N-sodium hydroxide at 100° for 3 hr., followed by esterification of the resulting syrup with ethereal diazomethane and then treatment with ethanolic methylamine, regenerated the crystalline methylamide. This methylamide (2·0 g.) was heated at 100° for 30 min. with N-sodium hydroxide (20 ml.), then cooled to −5° and acidified with 4N-sulphuric acid (7 ml.); the solution was extracted with chloroform (4 × 50 ml.); after being washed with water the chloroform extracts were evaporated to a syrup which was dissolved in 1% methanolic hydrogen chloride and kept at room temperature for 48 hr. Appropriate treatment gave *methyl* (*methyl*

4-O-*methyl*-α-D-*mannosid*)*uronate* as a syrup (1·5 g.), n_D^{17} 1·4727, $[\alpha]_D^{19}$ +84° (*c*, 1·0 in H_2O) (Found: C, 45·3; H, 7·3. $C_9H_{14}O_7$ requires C, 45·8; H, 6·8%). Methylation twice with methyl iodide and silver oxide, followed by treatment with ethanolic methylamine, gave methyl 2 : 3 : 4-tri-*O*-methyl-α-D-mannosiduronomethylamide, m. p. 103—105° alone or mixed with a specimen prepared by direct methylation of methyl α-D-mannopyranosiduronamide. After hydrolysis of the preceding ester (0·097 g.) with N-hydrochloric acid at 100° for 24 hr. in a sealed tube, oxidation with bromine water (7 days at 40°), esterification, distillation (b. p. 160—170°/0·1 mm.) and treatment with methanolic ammonia gave 2 : 3 : 4-*tri*-O-*methyl*-D-*mannardiamide* (0·030 g.) m. p. 192—193°, $[\alpha]_D^{18}$ −16° (*c*, 0·6 in H_2O) (Found: C, 38·0; H, 6·2; N, 12·5. $C_7H_{14}O_6N_2$ requires C, 37·8; H, 6·4; N, 12·6%).

Methyl 2 : 3 : 4-*Tri*-O-*methyl*-α-D-*mannosiduronomethylamide*.—Methyl α-D-mannopyranosiduronamide (1·99 g.) was methylated thrice with methyl iodide (23 ml.) and silver oxide (12 g.), dioxan being added as a solvent in the first operation. A colourless syrup (2·618 g., 103%), n_D^{15} 1·4661, which crystallised on trituration with light petroleum was obtained. After recrystallisation from light petroleum the *methylamide* had m. p. 103—105°, $[\alpha]_D^{19}$ +42° (*c*, 1·4 in H_2O) (Found: C, 50·4; H, 8·0; N, 4·8. $C_{11}H_{21}O_6N$ requires C, 50·2; H, 8·1; N, 5·3%). Hydrolysis with sodium hydroxide, esterification, and treatment with ethanolic methylamine regenerated it in good yield. Treatment of the methylamide (0·10 g.) with 2N-sodium hydroxide, then with N-hydrochloric acid, oxidation with bromine water, esterification, distillation of the derived ester (b. p. 130—140°/0·1 mm.), and treatment with methanolic ammonia gave the trimethylmannardiamide (0·030 g.), m. p. 211° (decomp.) unchanged by repeated recrystallisation from methanol or on admixture with a synthetic specimen prepared by Haworth, Hirst, Isherwood, and Jones (*J.*, 1939, 1878) which was now found to have m. p. 211° on the Kofler apparatus and in a capillary tube.

Methyl 2 : 3-*Di*-O-*methyl*-α-D-*glucopyranoside*.—Methyl α-D-glucopyranoside, m. p. 163—165° $[\alpha]_D^{17}$ +158° (*c*, 1·8 in H_2O) (100 g.), was converted into the 4 : 6-*O*-benzylidene derivative according to the method of Freudenberg *et al.* (*loc. cit.*). The crude product was extracted with boiling water (1500 ml.), and the aqueous extract filtered whilst hot. On cooling, the product was obtained as long needles (102 g., 70%), m. p. 164—165°, $[\alpha]_D$ +108° (Found: C, 59·0; H, 6·6. Calc. for $C_{14}H_{18}O_6$: C, 59·6; H, 6·4%). A solution of it (50 g.) in acetone (300 ml.) was methylated twice with aqueous 30% sodium hydroxide (320 ml.) and methyl sulphate (130 ml.) (Bell, *J.*, 1936, 859). Methyl 4 : 6-*O*-benzylidene-2 : 3-di-*O*-methyl-α-D-glucoside (51·5 g., 94%) had, after recrystallisation from ethanol, m. p. 121—122°, $[\alpha]_D$ +95° (Found: C, 61·8; H, 7·0. Calc. for $C_{16}H_{22}O_6$: C, 61·9; H, 7·2%). A solution of this (38·4 g.) in acetone (800 ml.) and 4N-sulphuric acid (200 ml.) was kept at room temperature until the rotation of the solution became constant, $[\alpha]_D$ +110° (72 hr.). After neutralisation (barium carbonate) the combined filtrate and washings were concentrated to a syrup from which benzaldehyde was removed by repeated distillation with water. The residue of methyl 2 : 3-di-*O*-methyl-α-D-glucopyranoside (23·5 g., 86%), recrystallised from carbon tetrachloride, had m. p. 81—82°, $[\alpha]_D^{18}$ +153° (*c*, 1·0 in H_2O) (Found: 48·9; H, 8·0. Calc. for $C_9H_{18}O_6$: C, 48·6; H, 8·1%).

Methyl (*Methyl* 2 : 3-*Di*-O-*methyl*-α-D-*glucopyranosid*)*uronate*.—The last mentioned glucoside (27·3 g.) dissolved in aqueous potassium hydroxide (14 g. in 2 l.) was stirred at room temperature and potassium permanganate (37 g.) added in small portions during 8 hr.; stirring was continued for a further 16 hr. Excess of permanganate was decomposed by aqueous potassium metabisulphite, the mixture filtered, and the residue washed with hot water (4 × 150 ml.). The combined filtrate and washings were neutralised with solid carbon dioxide and evaporated to dryness. The resultant white solid was extracted with ether (2 × 300 ml.) and then with boiling ethanol (3 × 300 ml.), and the ethanolic extracts were passed through a column (17 × 700 mm.) of Amberlite resin IR-120. The column was washed with water (200 ml.) and evaporation of the combined eluate and washings gave a syrup (20·5 g.) which was converted into the ester by treatment with 1% methanolic hydrogen chloride (500 ml.) at room temperature for 48 hr. Distillation of the product gave methyl (methyl 2 : 3-di-*O*-methyl-α-D-glucopyranosid)uronate as a syrup (20·9 g., 68%), b. p. 130—140°/0·5 mm., n_D^{18} 1·4441, $[\alpha]_D^{18}$ +111° (*c*, 1·1 in H_2O). The derived 4-*O*-*p*-nitrobenzoyl derivative (Smith, *J.*, 1940, 1035) (3·5 g. from 2·2 g.) had m. p. 156—158° alone or mixed m. p. with a specimen kindly supplied by Professor F. Smith, $[\alpha]_D$ +69° (Found: C, 51·4; H, 5·4; N, 4·1. $C_{17}H_{21}O_{10}N$ requires C, 51·1; H, 5·3; N, 3·5%). The derived uronophenylhydrazide, isolated as a crystalline residue (1·85 g.) after the ester (2·0 g.) had been heated with freshly distilled phenylhydrazine (0·78 ml.) in carbon dioxide in a sealed tube at 110° for 18 hr. and extracted with ether (3 × 20 ml.) under reflux, had m. p. 195—197° (from benzene), $[\alpha]_D$ +85°. Smith (*loc. cit.*) records m. p. 225—227°. The

mixed m. p., kindly determined by Professor F. Smith with his specimen, was 196—200°, 197° (after resolidification) (Found: C, 55·2; H, 6·8; N, 9·0. Calc. for $C_{15}H_{22}O_6N_2$: C, 55·2; H, 6·8; N, 8·6%). Hydrolysis of the methyl uronate with N-hydrochloric acid at 100° for 24 hr., followed by oxidation with bromine water, esterification, and distillation, gave syrupy 2 : 3-di-*O*-methyl-D-glucaro-1→4-lactone 6-methyl ester, b. p. 120—130°/0·1 mm., which crystallised after distillation and on recrystallisation from benzene had m. p. 99—100°, $[\alpha]_D^{18}$ +17° (*c*, 1·2 in H_2O). The derived amide had m. p. and mixed m. p. 154—155°. Two Purdie methylations of the methyl uronate (70 mg.), distillation, amide formation, and recrystallisation from benzene, gave 2 : 3 : 4-tri-*O*-methyl-α-D-glucosiduronamide, m. p. and mixed m. p. 180°, $[\alpha]_D^{18}$ +147° (*c*, 0·7 in H_2O).

Oxidation by Periodate.—Buffer solutions were prepared according to Vogel ("Quantitative Inorganic Analysis," Longmans Green and Co., London, 1939, p. 808), except that sodium salts were used in all experiments. The following buffer solutions were used (total molarity ~ 0·1M): A (pH 2·0), toluene-*p*-sulphonic acid–sodium toluene-*p*-sulphonate. B (pH 4·5), acetic acid–sodium acetate. C (pH 5·3), acetic acid–sodium acetate. D (pH 5·3), disodium hydrogen phosphate–sodium dihydrogen phosphate. E (pH 7·0), sodium dihydrogen phosphate–sodium hydroxide.

A typical oxidation is described in detail. The weighed substance (10—50 mg.; sufficient to give a back-titration difference of 10—20 ml.) was dissolved in about 40 ml. of the buffer solution at the correct temperature. 0·097M-Sodium metaperiodate (5 ml.) was added, the volume made up to 50 ml. with buffer solution, and the whole set aside in the dark at the appropriate temperature. At suitable intervals, portions of 10 ml. were saturated with sodium hydrogen carbonate, and 10 ml. of 0·1N-sodium arsenite and 1 g. of potassium iodide were added. This mixture was then set aside for 15 min. and finally titrated quickly with 0·1N-iodine (starch) until addition of 1 drop of iodine gave a blue colour which persisted for 5 sec. with shaking. A control experiment was conducted similarly. The detailed results for methyl α-D-galactopyranosiduronic methyl ester are given in Table 1 and the summarised results for all the derivatives oxidised are given in Table 2.

The authors are grateful to Dr. C. A. Beevers for examining the crystals of methyl 2 : 3 : 4-tri-*O*-benzoyl-6-*O*-triphenylmethyl-α-D-mannoside with the polarising microscope and by *X*-rays, and to Mr. H. Peglar for the preparation of some of the methyl α-D-mannoside from carob gum. They thank the University of Edinburgh for the award of a Vans Dunlop Scholarship, the Department of Scientific and Industrial Research for the award of a maintenance grant to one of them (R. A. E.), and the Distillers Company Limited for a grant.

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*Thiadiazoles. Part II.** 3 : 5-Diamino-1 : 2 : 4-thiadiazole and its 5-Alkyl Homologues.*

By FREDERICK KURZER.

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Some properties of 3 : 5-diamino-1 : 2 : 4-thiadiazole, consistent with its suggested structure, are described. The greater reactivity of the 3-amino-group is indicated by the preferential formation of 3-sulphonamido-derivatives. Under suitable conditions the parent compound forms di- and tri-acyl derivatives.

5-Alkylamino-3-amino-1 : 2 : 4-thiadiazoles are obtainable by the oxidative cyclisation of *N*-alkyl-*N'*-amidinothioureas, and yield mono-, di-, and tri-acyl derivatives.

AMIDINOTHIOUREA, when oxidised with iodine or hydrogen peroxide, is cyclised to 3 : 5-diamino-1 : 2 : 4-thiadiazole (II) (cf. Part I*): the oxidation of suitably substituted amidinothioureas and thiobiurets clearly opens a general route to various types of 1 : 2 : 4-thiadiazoles. Its applicability has now been confirmed, in the first place, by the synthesis 5-alkylamino-3-amino-1 : 2 : 4-thiadiazoles (VII). The oxidation of amidinothiourea by iodine is reversible and does not proceed to completion except in very dilute aqueous solution

* Part I, *J.*, 1955, 1.

(Part I): with *N*-alkyl-*N'*-amidinothioureas the position of equilibrium was still less favourable, so that iodine proved unsuitable as oxidising agent; hydrogen peroxide, however, effected the desired cyclisation readily.

N-Alkyl-*N'*-amidinothioureas, prepared by the method of Slotta, Tschesche, and Dressler (*Ber.*, 1930, **63**, 208), were isolated with advantage as highly crystalline arenesulphonates. Direct oxidation of these salts, by 6% hydrogen peroxide in boiling aqueous ethanol, afforded arenesulphonates of 5-alkylamino-3-amino-1 : 2 : 4-thiadiazole (VII) rapidly and in good yields. Small quantities of guanidine, formed as by-product, arose probably by the hydrolysis of the starting materials. In contrast to the parent compound (II) of this series, the 5-alkyl homologues (VII) proved alkali-resistant, so that the liberation of the free bases from their salts presented no difficulty.

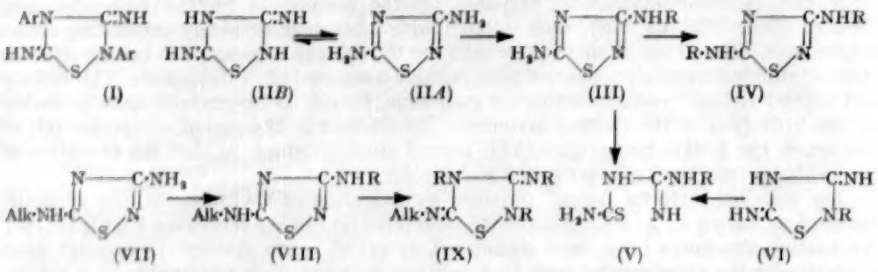
The so-called "Hector bases," obtained by oxidation of arylthioureas, are generally accepted as having 1 : 2 : 4-thiadiazolidine structures (I) (for references see Part I, *loc. cit.*). Alternative structures have been considered, however, in an attempt to account more explicitly for the experimental facts that only one imino-group is replaceable by a ketonic oxygen atom (Dost, *Ber.*, 1906, **39**, 863), or will undergo acylation. The formulæ of such monoacyl derivatives are as yet undecided (Bambas, "The Chemistry of Heterocyclic Compounds," Interscience Pub. Inc., New York, 1952, Vol. IV, p. 76). If the correctness of the structures (I) assigned to "Hector bases" is assumed, 3 : 5-diamino-1 : 2 : 4-thiadiazole (II) may be regarded as the parent compound of this series. It was therefore of interest to examine the behaviour of the simple compounds now synthesised towards acylating agents.

Interaction of equivalent quantities of sulphonyl chlorides and 3 : 5-diamino-1 : 2 : 4-thiadiazole afforded acidic monosubstitution products, which are regarded as 3-sulphonyl derivatives for the following reasons: Reduction, by nascent hydrogen, of the toluene-*p*-sulphonyl derivative to *N*-(toluene-*p*-sulphonylamidino)thiourea (V; R = *p*-$C_6H_4Me{\cdot}SO_2{\cdot}$) limits the site of the substitution (in the absence of rearrangement) to the 2- or the 3-position in the thiadiazole. The pronounced acidic nature of the sulphonyl derivatives favours the 3-sulphonamido-structure (III; R = $Ar{\cdot}SO_2$), since 2-sulphonyl compounds (VI; R = $Ar{\cdot}SO_2$) may be expected to be predominantly basic. The final decision in favour of structure (III) is supported by the analogous reaction of 2-aminothiazole which affords derivatives carrying the substituent on the extranuclear amino-group (2-sulphonamidothiazoles, *e.g.*, sulphathiazole; Fosbinder and Walter, *J. Amer. Chem. Soc.*, 1939, **61**, 2032; Lott and Bergum, *ibid.*, 3593).

Treatment of 3 : 5-diamino-1 : 2 : 4-thiadiazole with two equivalents of benzoyl chloride in pyridine gave an acidic disubstitution product; its formulation as the 3 : 5-dibenzamido-derivative (IV; R = Bz) is based on reasons similar to those given for the sulphonyl derivatives. However large an excess of acid chloride or anhydride was employed, four acyl residues could not be introduced into the molecule. Benzoyl chloride, for example, yielded a tribenzoyl derivative, the structure of which cannot be assigned with certainty at present. Acetic or propionic anhydride, on the other hand, afforded exceptionally sparingly soluble 3 : 5-diacylamino-derivatives (IV; R = Ac or Et·CO) which were instantly precipitated from the pyridine solution. However, their removal from the reacting phase is not likely to be the only reason for their failure to undergo further acylation, since substitution terminated similarly in the case of 3-amino-5-methylamino-1 : 2 : 4-thiadiazole with the formation of a pyridine-soluble monoacetyl derivative (formulated as VIII; Alk = Me, R = Ac).

For comparison, the corresponding acylation reactions of 5-alkylamino-3-amino-1 : 2 : 4-thiadiazoles were carried out, the methyl homologue (VII; Alk = Me) being used as the representative example. With one equivalent of benzoyl or sulphonyl halide, the expected monosubstituted derivatives were produced; they were strongly acidic and are regarded, in accordance with previous reasoning, as 3-substitution products (VIII; Alk = Me; R = Bz or *p*-$C_6H_4Me{\cdot}SO_2$). The action of larger proportions of benzoyl chloride produced mixtures of di- and tri-benzoyl derivatives, the latter being the sole products when a large excess of acid chloride was used; di- and tri-arenesulphonyl compounds were similarly obtained. Unlike all the other derivatives described, the triacylated

alkyl-1 : 2 : 4-thiadiazoles were not acidic. In view of the greater difficulty of introducing acyl groups into acylamino- than into unsubstituted amino(or imino)-residues, the absence of diacylamino-groups in all derivatives may reasonably be assumed. The tribenzoyl and



trisulphonyl derivatives of (VII) are therefore formulated as substituted 1 : 2 : 4-thiadiazolidines (IX; Alk = Me; R = Bz or *p*-$C_6H_4Me{\cdot}SO_2$), although a possible 2-acyl-5-acylalkylamino-3-acylimino-2 : 3-dihydro-1 : 2 : 4-thiadiazole structure is not fully excluded. A decision concerning the structure of the diacyl products must be deferred.

The failure of 3 : 5-diamino-1 : 2 : 4-thiadiazole to yield tetra-acyl derivatives under the usual conditions, and the varied behaviour of 1 : 2 : 4-thiadiazoles on acylation in general, suggests that the observed exclusive monoacylation of " Hector bases " is no decisive bar to their having thiadiazolidine structures (I). The greater reactivity of the 3-amino-group in (II) now demonstrated seems to justify the expectation that the acyl derivatives of " Hector bases " are 3-acylated structures.

The presence of substituents in 3 : 5-diamino-1 : 2 : 4-thiadiazole exerts a considerable stabilising influence on the heterocyclic ring system. Thus, sulphur dioxide rapidly opened the nucleus of the parent compound (II) under the mildest conditions with regeneration of amidinothiourea, but did not attack the 3-sulphonyl derivatives (III). Similarly, alkaline hydrolysis quickly converted the 3 : 5-diamino-compound (II) into amidinourea (equation 1) (the eliminated sulphur being simultaneously removed as soluble alkali polysulphide), but failed to bring about the corresponding degradation of the 5-alkyl homologues (VII). Alkaline sodium plumbite desulphurised 3 : 5-diamino-1 : 2 : 4-thiadiazole instantly on warming, or slowly even at room temperature. Its acyl derivatives released sulphur only when boiled with sodium plumbite containing a large excess of alkali, while 5-alkylamino-3-amino-1 : 2 : 4-thiadiazoles and their derivatives resisted desulphurisation entirely.

$$C_2H_4N_4S\ (II) + H_2O \longrightarrow NH_2{\cdot}C(:NH){\cdot}NH{\cdot}CO{\cdot}NH_2 + S \quad . \quad . \quad . \quad (1)$$

The synthesis of 3 : 5-diamino-1 : 2 : 4-thiadiazole has been simplified by oxidising amidinothiourea, in dilute mineral acid at moderate temperatures, with " Perhydrol." A similar procedure had been successfully used in the oxidative cyclisation of dithiobiuret (Preisler and Bateman, *J. Amer. Chem. Soc.*, 1947, **69**, 2632). In a slightly higher temperature range, however, " Perhydrol " converted amidinothiourea into amidinourea; this desulphurisation proceeds probably by way of primarily formed thiadiazole (II), since this base is also rapidly converted into amidinourea under identical conditions.

Both amidinothioureas and 1 : 2 : 4-thiadiazoles derived therefrom formed sparingly soluble monopicrates which were suitable for recovering small quantities of the bases from dilute solution; those prepared from thiadiazoles had m. p.s ranging sufficiently widely to allow their use for identification purposes.

Experimental

Light petroleum was of boiling range 60—80°. The 5-alkylamino-3-amino-1 : 2 : 4-thiadiazole sulphonates were, in general, considerably more soluble in 96% than in absolute ethanol; unless otherwise specified, the former grade was used.

3 : 5-*Diamino*-1 : 2 : 4-*thiadiazole*.—A solution of amidinothiourea (11·8 g., 0·1 mole) in

2N-hydrochloric acid (50 ml., 0·1 mole) at 20° was treated with hydrogen peroxide (30% w/v; 34 ml., 0·3 mole) in three portions at 3-min. intervals. The resulting clear colourless solution was kept at 35° during 30 min. (external cooling). Toluene-*p*-sulphonic acid monohydrate (23·75 g., 0·125 mole) was then added to the stirred liquid and dissolved instantly, while a copious crystalline precipitate of 3 : 5-diamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate appeared. The suspension was immediately cooled to 0° in a freezing mixture, to avoid a possible rapid spontaneous rise in temperature, resulting in the conversion of the material into amidinourea. The salt was collected at 0° [m. p. 236—238° (decomp.); 21—23 g., 73—80%] and purified as before (cf. Part I, *loc. cit.*).

Interaction of the above reactants at 60—70° yielded only amidinourea toluene-*p*-sulphonate (10—15 g., 36—55%).

3 : 5-*Diamino*-1 : 2 : 4-*thiadiazole.*—*Reduction.* A solution of 3 : 5-diamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate (1·44 g., 0·005 mole) in water (10 ml.) at 65° was treated with a slow stream of sulphur dioxide during 20 min., followed by toluene-*p*-sulphonic acid monohydrate (0·95 g., 0·005 mole). The large prisms which separated on cooling to 0° (1·32 g., 91%) were amidinothiourea toluene-*p*-sulphonate, m. p. (after crystallisation from ethanol) and mixed m. p. 177—178° (decomp.).

Alkaline hydrolysis. A solution of the toluene-*p*-sulphonate (2·88 g., 0·01 mole) in aqueous sodium hydroxide (12%; 7 ml., 0·02 mole) was boiled during 3 min. The cooled orange liquid, on acidification with concentrated hydrochloric acid (2·5 ml., 0·025 mole), evolved hydrogen sulphide, and gave a granular precipitate of sulphur (0·19 g., 60%). The decanted liquid was filtered (carbon) while hot, and the clear filtrate treated with toluene-*p*-sulphonic acid monohydrate (0·95 g., 0·005 mole). On partial spontaneous evaporation, lustrous prisms [m. p. 226—232° (decomp.); 1·95 g., 72%] of amidinourea toluene-*p*-sulphonate, m. p. and mixed m. p. 238—240° (decomp.) (from 90% aqueous ethanol) were deposited.

Further interaction with hydrogen peroxide. A suspension of the powdered toluene-*p*-sulphonate (4·3 g., 0·015 mole) in N-hydrochloric acid (15 ml., 0·015 mole) was treated with hydrogen peroxide (30%; 5 ml., 0·045 mole) and warmed to 50°. The temperature of the resulting solution was thereupon maintained at 60—65° by external cooling. When no further spontaneous temperature rise occurred (20—30 min.), the solution was set aside at 0° overnight. The separated prisms (2·15—2·5 g., 52—61%) were amidinourea toluene-*p*-sulphonate, m. p. and mixed m. p. 238—240° (decomp.) (from 90% ethanol).

3 : 5-*Di*(*acetamido*)-1 : 2 : 4-*thiadiazole.*— A solution of 3 : 5-diamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate (2·88 g., 0·01 mole) in anhydrous pyridine (15 ml.) was treated with acetic anhydride (6·12 g., 0·06 mole), and the resulting hot (50°) solution heated on the steam-bath. Already after 2—3 min., a white crystalline solid separated. Heating was continued for 30 min., the suspension stirred into N-hydrochloric acid (150 ml.), and the white product collected and washed with water [m. p. 310—315° (decomp.); 1·77—1·90 g., 88—95%]. Two crystallisations from glacial acetic acid (100 ml. per g., recovery 90%) gave lustrous needles of 3 : 5-*di*(*acetamido*)-1 : 2 : 4-*thiadiazole*, m. p. 314—316° (decomp., after sintering slightly at 305°) (Found: C, 36·1; H, 4·0; N, 28·5; S, 16·5. $C_6H_8O_2N_4S$ requires C, 36·0; H, 4·0; N, 28·0; S, 16·0%), insoluble in boiling ethanol, benzene, chloroform, or dioxan, soluble in boiling glacial acetic acid, nitrobenzene, or in cold alkalis, and reprecipitated therefrom by acids.

3 : 5-*Di*(*propionamido*)-1 : 2 : 4-*thiadiazole*, similarly prepared, separated from the hot pyridine solution as above [m. p. 288—290° (decomp., previously sintering at 270°); 85%]. Two crystallisations from boiling ethanol (200 ml. per g., recovery 80%) gave needles, m. p. 292—293° (decomp., becoming brown at 280—285°) (Found: C, 42·1; H, 5·6; N, 25·1. $C_8H_{12}O_2N_4S$ requires C, 42·1; H, 5·3; N, 24·6%), very sparingly soluble in boiling water and ethanol.

3 : 5-*Di*(*benzamido*)-1 : 2 : 4-*thiadiazole.*—A solution of 3 : 5-diamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate (2·88 g., 0·01 mole) in pyridine (20 ml.), treated with benzoyl chloride (3·1 g., 0·022 mole), was kept at 100° during 30 min. The crystalline precipitate obtained on pouring the liquid into 2N-hydrochloric acid (120 ml.) at 0° was collected, heated with water (50 ml.) to 100° (to remove benzoic acid), and filtered (m. p. 256—260°; 2·60 g., 80%), and the solid twice crystallised from ethanol (100 ml. per g.; recovery per crystallisation, 85%), yielding 3 : 5-*di*(*benzamido*)-1 : 2 : 4-*thiadiazole*, as needles, m. p. 263—265° (Found: C, 58·6; H, 4·1; N, 16·9; S, 9·4. $C_{16}H_{12}O_2N_4S$ requires C, 59·3; H, 3·7; N, 17·3; S, 9·9%), soluble in warm alkalis and reprecipitated by acids.

Tribenzoyl Derivative of 3 : 5-*Diamino*-1 : 2 : 4-*thiadiazole.*—Treatment of 3 : 5-diamino-1 : 2 : 4-thiadiazole (0·01 mole) with an excess of benzoyl chloride (7·05 g., 0·05 mole) gave,

by the above procedure, a granular solid (4·6 g.). Three crystallisations from ethanol (30 ml. per g.) gave prisms of the *tribenzoyl derivative*, m. p. 219—221° (yield, including material from the mother-liquors, 2·9—3·5 g., 68—81%) [Found: C, 64·1; H, 4·1; N, 13·4; S, 7·25%; *M* (cryoscopically, in naphthalene), 380. $C_{23}H_{16}O_3N_4S$ requires C, 64·5; H, 3·7; N, 13·1; S, 7·5%; *M*, 428], soluble in warm alkalis and reprecipitated by acids.

Small quantities (up to 8%) of the dibenzoyl derivative, m. p. 263—265°, formed as by-product in some experiments, were removed by fractional crystallisation.

The use of a large excess (8 equiv.) of benzoyl chloride did not introduce a fourth benzoyl residue, but afforded the tribenzoyl derivative exclusively in 85—90% yield.

*5-Amino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole.*—A solution of 3 : 5-diamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate (8·64 g., 0·03 mole) in pyridine (30 ml.), treated with toluene-*p*-sulphonyl chloride (6·3 g., 0·033 mole), was heated on the steam-bath during 30 min. The white semicrystalline precipitate obtained on addition of the pyridine solution to N-hydrochloric acid (120 ml.) at 0° was collected, air-dried (m. p. 228—232°, after sintering at 220°; 6·9 g., 85%), and crystallised by dissolution in ethanol (20 ml.)–acetone (60 ml.), followed by addition of light petroleum (120 ml.); prisms of *5-amino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole*, m. p. 231—233° (decomp., after sintering at 228°), were deposited (Found: C, 40·3; H, 3·9; N, 20·5; S, 23·5. $C_9H_{10}O_3N_4S_2$ requires C, 40·0; H, 3·7; N, 20·7; S, 23·7%). The material dissolved in dilute alkalis and was reprecipitated by acids.

*5-Amino-3-*m*-nitrobenzenesulphonamido-1 : 2 : 4-thiadiazole* was similarly prepared. The precipitated crude powder dissolved readily in boiling acetone, and was deposited therefrom, on cooling and partial evaporation, as a pale yellow powder [m. p. 258—264° (decomp., after sintering at 240°); 62%], now almost insoluble in the usual solvents. Two crystallisations from boiling nitrobenzene afforded pale yellow prisms of the solvated derivative, m. p. 274—276° (decomp., after sintering at 260°). Removal of the nitrobenzene of crystallisation, by keeping the solvate at 210—230° during 30 min., gave the microcrystalline derivative, m. p. 274—276° (decomp., after sintering at 270°) (Found: C, 32·1; H, 2·25; N, 23·2; S, 20·8. $C_8H_7O_4N_5S_2$ requires C, 31·9; H, 2·3; N, 23·25; S, 21·3%).

*5-Amino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole.—Reduction.* A boiling solution of the reactant (2·70 g., 0·01 mole) in ethanol (40 ml.) containing zinc foil (4 g.) was treated dropwise with concentrated hydrochloric acid (4 ml.) during 1 min.; after the initial vigorous reaction, the suspension was gently refluxed during 15 min. The liquid was decanted from the zinc (which was again extracted with a little boiling ethanol), and the combined clear solution evaporated in a vacuum to small volume (10 ml.). After storage at 0° during 24 hr., the white crystalline solid was collected, twice stirred with N-hydrochloric acid (2 × 5 ml.) [to remove zinc salt], filtered off, and washed with cold water. The air-dried product (m. p. 198—202°, after sintering at 185°; 2·25 g., 82%) gave, on crystallisation from ethanol (10 ml. per g.), prisms of *N*-(toluene-*p*-sulphonylamidino)thiourea, m. p. and mixed m. p. (cf. Kurzer and Powell, *J.*, 1953, 2531) 201—202° (decomp.) (Found: C, 40·0; H, 4·6; N, 20·8. Calc. for $C_9H_{12}O_3N_4S_2$: C, 39·7; H, 4·4; N, 20·6%).

5-Amino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole, dissolved in boiling ethanol–acetone, was recovered unchanged after treatment with sulphur dioxide during 1 hr.

5-Alkylamino-3-amino-1 : 2 : 4-thiadiazoles.

*N-Alkyl-N′-amidinothiourea Toluene-*p*-sulphonates.*—*N*-Alkyl-*N′*-amidinothioureas, prepared by the method of Slotta, Tschesche, and Dressler (*Ber.*, 1930, **63**, 208), were conveniently isolated as toluene-*p*-sulphonates as follows: The solution obtained after refluxing guanidine thiocyanate and methyl *iso*thiocyanate (0·15 mole each) in ethanolic sodium ethoxide (90 ml., containing 0·15 g.-atom of sodium) for 1 hr., was quickly evaporated to approx. half its bulk under reduced pressure. Dilution with hot water (25 ml.) redissolved the separated crystalline solid; the warm solution was filtered to remove flocculent impurities, and the filtrate treated with toluene-*p*-sulphonic acid monohydrate (38·1 g., 0·2 mole) and set aside at 0°. The separated crystals were collected at 0°, and successively washed with ice-water (2 × 10 ml.) and ethanol (15 ml.). The dry product (32—35 g.) was refluxed with ethanol (40 ml.), and a small quantity of insoluble material (3—4 g.) filtered off at the pump while hot. The product which separated from the filtrate on cooling to 0° was twice recrystallised from ethanol (1·5 ml. per g.) and formed white opaque prisms of *N-amidino-N′-methylthiourea toluene-*p*-sulphonate*, m. p. 160—162° (decomp.) (total yield, including material from the mother-liquors, 25—29·5 g., 55—65%) (Found: C, 39·2; H, 5·3; N, 17·9. $C_{10}H_{16}O_3N_4S_2$ requires C, 39·5; H, 5·3; N, 18·4%).

By the same method, N-*amidino*-N′-*ethylthiourea toluene*-p-*sulphonate* was obtained (45—55%) as opaque prisms (from ethanol; 3 ml. per g.), m. p. 139—141° (decomp.) (Found: C, 41·7; H, 5·85; N, 16·8. $C_{11}H_{18}O_3N_4S_2$ requires C, 41·5; H, 5·7; N, 17·6%).

The same procedure gave N-*amidino*-N′-n-*propylthiourea toluene*-p-*sulphonate* (45%) as prisms, m. p. 137—139° (decomp.) (Found: C, 43·6; H, 5·8; N, 16·2. $C_{12}H_{20}O_3N_4S_2$ requires C, 43·4; H, 6·0; N, 16·9%).

3-*Amino*-5-*methylamino*-1 : 2 : 4-*thiadiazole*.—A solution of *N*-amidino-*N*′-methylthiourea toluene-*p*-sulphonate (6·08 g., 0·02 mole) in boiling ethanol (35 ml.) was treated with hydrogen peroxide (6%; 34·5 ml., 0·06 mole) in three equal portions at 3-min. intervals. The resulting solution was rapidly evaporated to approximately half its volume in a vacuum, and the residual clear liquid treated with toluene-*p*-sulphonic acid monohydrate (1·90 g., 0·01 mole). The crystals separating on storage at 0° were collected (m. p. 174—177°; 3·75 g., 62%) [aqueous filtrate, A] and crystallised from boiling ethanol (8 ml. per g.; recovery, 75%), affording prisms of 3-*amino*-5-*methylamino*-1 : 2 : 4-*thiadiazole toluene*-p-*sulphonate*, m. p. 177—179° (decomp.) (Found: C, 39·9; H, 4·8; N, 18·2; S, 20·75. $C_{10}H_{14}O_3N_4S_2$ requires C, 39·7; H, 4·6; N, 18·5; S, 21·2%).

The aqueous filtrates A, on spontaneous evaporation to small volume (10 ml.), gave large lustrous prisms (m. p. 222—224°; 0·4—0·6 g., 8—13%), which consisted of guanidine toluene-*p*-sulphonate, m. p. and mixed m. p. 225—228° (from ethanol).

The (crude) toluene-*p*-sulphonate (3·02 g., 0·01 mole) was warmed with aqueous sodium hydroxide (12%; 6·7 ml., 0·02 mole) to about 40°; on cooling, the clear liquid rapidly deposited minute needles, which were collected at 0°, washed with a few drops of water [m. p. 156—162°; 0·98 g., 75%], and twice crystallised from ethanol–light petroleum (10 and 4 ml. respectively, per g.; recovery per crystallisation, 70—80%). The 3-*amino*-5-*methylamino*-1 : 2 : 4-*thiadiazole* formed needles, m. p. 158—159° [Found: C, 28·1; H, 4·55; N, 43·0; S, 24·4%; *M* (Rast), 135, 145; (cryoscopically, in thymol) 130, 135. $C_3H_6N_4S$ requires C, 27·7; H, 4·6; N, 43·1; S, 24·6%; *M*, 130].

3-*Amino*-5-*ethylamino*-1 : 2 : 4-*thiadiazole*.—Oxidation of *N*-amidino-*N*′-ethylthiourea toluene-*p*-sulphonate (6·35 g., 0·02 mole) by the above procedure gave a product [m. p. 138—140° (decomp.); 4·1—4·75 g., 65—75%], which on crystallisation from ethanol–light petroleum (5 and 2 ml. per g., respectively; recovery 60%) formed prisms of 3-*amino*-5-*ethylamino*-1 : 2 : 4-*thiadiazole toluene*-p-*sulphonate*, m. p. 140—142° (decomp.) (Found: C, 41·6; H, 5·0; N, 17·8; S, 19·9. $C_{11}H_{16}O_3N_4S_2$ requires C, 41·8; H, 5·1; N, 17·7; S, 20·25%). Small yields of guanidine toluene-*p*-sulphonate were again isolated from the appropriate aqueous filtrates (see above).

The crude salt (3·16 g., 0·01 mole) was dissolved in aqueous sodium hydroxide (4%; 20 ml., 0·02 mole) at 80°. The filtered clear solution deposited prisms, which were collected at 0° (m. p. 174—176; 1·15 g., 80%). Crystallisation from ethanol (10 ml. per g., recovery 60%) gave 3-*amino*-5-*ethylamino*-1 : 2 : 4-*thiadiazole*, m. p. 177—179° (Found: C, 33·4; H, 5·4; N, 37·9; S, 22·0. $C_4H_8N_4S$ requires C, 33·3; H, 5·6; N, 38·9; S, 22·2%).

3-*Amino*-5-n-*propylamino*-1 : 2 : 4-*thiadiazole*.—Oxidation of *N*-amidino-*N*′-*n*-propylthiourea toluene-*p*-sulphonate (0·015 mole) in boiling ethanol (30 ml.) with hydrogen peroxide (6%; 0·045 mole) during 15 min., followed by rapid vacuum evaporation to 30 ml., gave a colourless liquid, which was made strongly alkaline (at 0—5°) with sodium hydroxide (20% w/v; 6 ml., 0·03 mole). Separation of the product was completed by spontaneous evaporation, at room temperature, to 15—20 ml. The collected (0°) crude product (1·23 g., 52%) gave, after two crystallisations from water (6 ml. per g.), prismatic needles of 3-*amino*-5-n-*propylamino*-1 : 2 : 4-*thiadiazole*, m. p. 146—148° (Found: C, 38·15; H, 6·15; N, 34·7; S, 19·9. $C_5H_{10}N_4S$ requires C, 38·0; H, 6·3; N, 35·4; S, 20·25%).

The *toluene*-p-*sulphonate*, prepared from equivalent proportions of the above base and toluene-*p*-sulphonic acid in hot saturated aqueous solution, formed prisms, m. p. 110—112° (decomp.) (from ethanol–light petroleum) (Found: C, 43·6; H, 5·5. $C_{12}H_{18}O_3N_4S_2$ requires C, 43·6; H, 5·45%).

Picrates.—Amidinothiourea and 1 : 2 : 4-thiadiazole picrates were prepared in 70—95% yield from equivalent quantities of picric acid and the requisite toluene-*p*-sulphonate (except in the case of amidinothiourea, where the free base was used) in saturated aqueous or ethanolic solution. The results are summarised in the Table.

3-*Acetamido*-5-*methylamino*-1 : 2 : 4-*thiadiazole*.—3-Amino-5-methylamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate (1·50 g., 0·005 mole), dissolved in pyridine (6 ml.), was heated with acetic anhydride (6·1 g., 0·06 mole) on the steam-bath during 1 hr., and the yellow liquid diluted with water (40 ml.) and acidified to Congo-red with concentrated hydrochloric acid (10 ml.).

On partial evaporation at room temperature, the solution deposited massive needles [m. p. 245—248° (decomp., after sintering at 240°); 0·72 g., 84%]. Crystallisation from boiling water–ethanol (4 : 1, 100 ml. per g.) gave needles of *3-acetamido-5-methylamino-1 : 2 : 4-thiadiazole*,

Amidinothiourea picrates R·NH·CS·NH·C(:NH)·NH_2,$C_6H_3O_7N_3$.

R	Medium [a]	Crystn. [b]	M. p. [c]	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
H	i	A	208—209°	$C_9H_9O_7N_7S$	28·2	2·6	27·7	2·6
Me	ii	A	224—226	$C_{10}H_{11}O_7N_7S$	30·3	3·0	29·9	3·0
Et	ii	A	223—225	$C_{11}H_{13}O_7N_7S$	32·0	3·7	32·0	3·5
Pr[a]	ii	A	218—219	$C_{11}H_{15}O_7N_7S$	34·2	3·9	33·9	3·85

3 : *5-Disubstituted* 1 : 2 : 4-*thiadiazole picrates* 5-R·NH·$C_2H_2N_3S$,$C_6H_3O_7N_3$ [cf. (VII)].

H	i	A	230—232	$C_9H_7O_7N_7S$	28·0	2·3	27·8	2·0
Me	i	B	227—228	$C_9H_9O_7N_7S$	30·3	2·5	30·1	2·5
Et	i	C	169—171	$C_{10}H_{11}O_7N_7S$	32·6	2·85	32·2	2·95
Pr[a]	i	A	171—173	$C_{11}H_{13}O_7N_7S$	33·9	3·3	34·1	3·4

[a] Prepared (i) in saturated boiling H_2O, (ii) in saturated boiling 96% EtOH. [b] Crystallised (A) from 60% EtOH, (B) from EtOH–acetone, (C) from EtOH–light petroleum. [c] All picrates decomposed on melting.

m. p. 248—251° (decomp., after sintering at 240—245°) (Found: C, 34·9; H, 4·5; N, 31·8; S, 17·9. $C_5H_8ON_4S$ requires C, 34·9; H, 4·65; N, 32·6; S, 18·6%).

3-Benzamido-5-methylamino-1 : 2 : 4-thiadiazole was similarly prepared from equimolar proportions of the thiadiazole toluene-*p*-sulphonate and benzoyl chloride in pyridine (40%), and after crystallisation from ethanol, consisted of prisms, m. p. 201—203° (Found: C, 51·7; H, 3·9. $C_{10}H_{10}ON_4S$ requires C, 51·3; H, 4·3%).

Di- and Tri-benzoyl Derivatives.—Treatment, as above, of the thiadiazole toluene-*p*-sulphonate (0·005 mole) with three equiv. of benzoyl chloride gave a crude product (1·75 g.), which was boiled with ethanol (25 ml.). The ethanol-insoluble fraction (0·62 g., 28%) (filtrate A) was twice crystallised from ethanol–benzene (1 : 1; 40 ml. per g.) and gave prisms of *2 : 4-dibenzoyl-3-benzoylimino-5-methylimino-1 : 2 : 4-thiadiazolidine*, m. p. 199—200° (Found: C, 65·5; H, 3·9; N, 12·4; S, 7·4. $C_{24}H_{18}O_3N_4S$ requires C, 65·2; H, 4·1; N, 12·7; S, 7·2%). The ethanolic filtrates A contained a product, which consisted, after recrystallisation from ethanol–light petroleum, of prisms (0·85 g., 50%) of the *dibenzoyl derivative*, m. p. 182—185° (Found: C, 61·1; H, 4·05. $C_{17}H_{14}O_2N_4S$ requires C, 60·35; H, 4·1%). The use of 8 molar proportions of benzoyl chloride gave the tribenzoyl derivative, m. p. 199—200°, exclusively in 85% yields.

*5-Methylamino-3-toluene-*p*-sulphonamido-1 : 2 : 4-thiadiazole* was prepared from equimolecular proportions of the reactants in pyridine in the usual manner (see above). The crude product was twice crystallised from acetone–ethanol (1 : 1; approx. 100 ml. per g.) and gave prisms, m. p. 254—256° (yield, including material from the mother-liquors, 80%) (Found: C, 42·15; H, 4·2; N, 19·2; S, 22·3. $C_{10}H_{12}O_2N_4S_2$ requires C, 42·25; H, 4·2; N, 19·7; S, 22·5%). The material dissolved in dilute alkalis and was reprecipitated by acids.

Di- and Tri-arenesulphonyl Derivatives.—Treatment of 3-amino-5-methylamino-1 : 2 : 4-thiadiazole toluene-*p*-sulphonate (1·50 g., 0·005 mole) with toluene-*p*-sulphonyl chloride (3·80 g., 0·02 mole) in anhydrous pyridine (10 ml.) at 100° during 30 min., followed by addition of the orange liquid to ice–hydrochloric acid, gave a crude product which was briefly boiled with ethanol (30 ml.). The undissolved white solid was quickly collected (ethanolic filtrate A) [m. p. 200—208°; 0·45 g., 15%] and afforded, after two crystallisations from acetone–ethanol (25 ml. each per g.), prisms of *5-methylimino-3-toluene-*p*-sulphonylimino-2 : 4-ditoluene-*p*-sulphonyl-1 : 2 : 4-thiadiazolidine*, m. p. 210—212° (Found: C, 48·2; H, 4·05; N, 9·8; S, 22·2. $C_{24}H_{24}O_6N_4S_4$ requires C, 48·65; H, 4·05; N, 9·5; S, 21·6%), insoluble in caustic alkalis.

The ethanol filtrates A deposited a crystalline solid on storage at 0°. Two crystallisations from boiling ethanol (15 ml. per g.) [a trace of insoluble material being quickly filtered off in each crystallisation] gave platelets of the *ditoluene-*p*-sulphonyl derivative*, m. p. 171—173° (yield, including material from the mother-liquors, 1·15 g., 52%) (Found: C, 46·3; H, 3·9; N, 12·8; S, 21·8. $C_{17}H_{18}O_4N_4S_3$ requires C, 46·6; H, 4·1; N, 12·8; S, 21·9%), sparingly soluble in very dilute alkalis and reprecipitated by mineral acids.

The use of 8 molar proportions of sulphonyl chloride did not substantially alter the relative amounts of tri- and di-sulphonyl derivatives isolated.

Sodium Plumbite Tests.—Solutions or suspensions of the appropriate product (0·1 g.) in 6, 12, or 20% aqueous sodium hydroxide (3 ml.) containing 3 drops of 10% lead acetate were

boiled during 2 min. The following compounds gave immediate copious precipitates of lead sulphide in 6% sodium hydroxide: *N*-alkyl-*N'*-amidinothioureas (alkyl = Me, Et, Pr^{i}); (toluene-*p*-sulphonylamidino)thiourea (V; R = *p*-$C_6H_4Me{\cdot}SO_2$). The following gave small precipitates slowly on boiling: In 6% sodium hydroxide: (IV; R = Ac or Et·CO). In 12% sodium hydroxide: (IV; R = Bz); tribenzoyl derivative of (II). In 20% sodium hydroxide: (VII; Alk = Me). The following compounds did not give any lead sulphide in boiling 20% sodium hydroxide during 3 min.: (VII; Alk = Et or Pr^{n}); (VIII; Alk = Me, R = Ac or *p*-$C_6H_4Me{\cdot}SO_2$); (IX; Alk = Me, R = Bz or *p*-$C_6H_4Me{\cdot}SO_2$); dibenzoyl and ditoluene-*p*-sulphonyl derivatives of (VII; Alk = Me).

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Liquid-phase Reactions at High Pressure. Part IX. The Polymerisation of Some 1 : 2-Disubstituted Ethylenes.*

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The peroxide-catalysed polymerisation of twelve 1 : 2-disubstituted ethylenes at hydrostatic pressures up to 10,000 atm. has been examined. Five of these substances, which do not polymerise readily or at all at ordinary pressures, give high yields of polymer under the conditions employed.

The modes by which pressure may accelerate the polmerisation are discussed. In two cases failure to react, or to proceed beyond the dimer, is attributed to steric hindrance, and in the case of *tert.*-butyl cinnamate it is probable that steric hindrance occurs but is reduced at high pressures. The relation of polymerisability to the index of free valence is considered in a number of cases.

HIGH pressures are known to accelerate the polymerisation of olefins, and to favour higher polymers. The effect has been extensively studied, but little attention has been paid to 1 : 2-disubstituted ethylenes, which are much less readily polymerisable at ordinary pressures than are olefins which contain the $=CH_2$ grouping. The peroxide-catalysed polymerisation of twelve substances of this class has now been investigated at pressures up to 10,000 atm., and the results are correlated with the structure of the monomer.

Compounds of this kind previously investigated include 1 : 2-dichloroethylene (Weale, *J.*, 1952, 2223), crotonaldehyde (Klaasens and Gisholf, *J. Polymer Sci.*, 1953, **10**, 149), diethyl fumarate (Starkweather, *J. Amer. Chem. Soc.*, 1934, **56**, 1870), indene (Bridgman and Conant, *Proc. Nat. Acad. Sci.*, 1929, **15**, 680; U.S.P. 1,953,116; Fr.P. 699,555; Tammann and Pape, *Z. anorg. Chem.*, 1931, **200**, 113; Klaasens and Gisholf, *loc. cit.*), ethyl cinnamate (Sapiro, Linstead, and Newitt, *J.*, 1937, 1784), and *cyclo*hexene (Zelinskii and Vereshchagin, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1954, **44**; Nemtzov, Nizokina, and Soskina, *J. Gen. Chem. U.S.S.R.*, 1938, **8**, 1303).

The last four compounds have been further studied, and they are listed with the other monomers used in the following section, which briefly summarises the extent to which the compounds undergo thermal and peroxide-catalysed polymerisation at ordinary pressures. Some results are included for ionic polymerisation at 1 atm.

At normal pressure, the thermal polymerisation of *cyclo*hexene yields dimers and trimers, and small quantities of higher polymers (Nemtzov *et al.*, *loc. cit.*; Lecomte, Leendertse, and Waterman, *Compt. rend.*, 1947, **224**, 193) and with benzoyl peroxide low

* Part VIII, *J.*, 1954, 2959.

polymers containing benzoyloxy-groups are formed (Kaishi Noma and Takashi Tsuchida, *Chem. High Polymers, Japan*, 1948, **5**, 166). For stilbene, quantitative data are lacking, but it has been shown to form small amounts of low polymer (*e.g.*, Schildknecht, "Vinyl and Related Polymers," John Wiley & Sons, Inc., New York, 1952, p. 156). Indene has been more widely studied. Thermal polymerisation in the range 120—175° is a first-order reaction, producing polymers of a wide range of molecular weights (Bergmann and Taubadel, *Ber.*, 1932, **65**, 463; Dostal and Raff, *Z. phys. Chem.*, 1936, **32**, *B*, 417; Breitenbach, *Z. Elektrochem.*, 1937, **43**, 323; Corrin, *J. Polymer Sci.*, 1947, **2**, 257; Schmid and Gutman, *ibid.*, 1948, **3**, 325). Analysis of a sample of polyindene gave molecular weights in the range 200—1200 (Pass, *ibid.*, p. 327).

Using $SbCl_5$ and $SnCl_4$ as catalysts, Whitby and Katz (*J. Amer. Chem. Soc.*, 1928, **50**, 1160) obtained polymers corresponding to the formula $(C_9H_8)_{39}$ and found that the molecular weight decreased with higher reaction temperatures. They also report a relation between the melting point of the polymer fraction and its molecular weight. Marvel and McCain (*ibid.*, 1953, **75**, 3272) produced up to 10% of polymerisation by heating ethyl cinnamate with benzoyl peroxide or αα′-azobis*iso*butyronitrile at 60° for one month. Methyl cinnamate under similar conditions for 13 days yielded 2% of polymer. The molecular weights were 7600 and 2300, respectively.

Diethyl and dimethyl maleate, treated in turn with large quantities of benzoyl peroxide ($\frac{1}{2}$—$\frac{1}{3}$ mol.), at 53° for 700 hr. yielded polymers with an average chain length of four monomer units (Marvel *et al.*, *ibid.*, 1947, **69**, 52). Diethyl fumarate in the presence of αα′-azo*iso*butyronitrile gave some polymer (Walling and McElhill, *ibid.*, 1951, **73**, 2819).

Crawford has studied the polymerisation of methyl α-*tert.*-butylacrylate (Crawford and Smith, *J.*, 1952, 1220; Crawford, *J.*, 1953, 2658). Small amounts of low polymer were formed on exposure to ultraviolet light or on reaction with benzoyl peroxide. The yield of dimer was increased by the action of sodium in liquid ammonia.

There are no data for the polymerisation of maleic anhydride, except as a copolymer; and 1 : 2-dibromoethylene, *n*-butyl cinnamate, and *tert.*-butyl cinnamate have apparently not been polymerised.

Experimental

Apparatus.—The high-pressure apparatus used was essentially that described in previous papers in this series (Newitt, Linstead, Sapiro, and Boorman, *J.*, 1937, 876; Raistrick, Sapiro, and Newitt, *J.*, 1939, 1761), a steel container replacing the glass reaction tube at pressures above 5000 atm.

Materials and Procedure.—The conditions of reaction and molecular weights are recorded in Table 2.

Benzoyl peroxide (B.D.H.) for use as catalyst was purified by Augood, Hey, and Williams's method (*J.*, 1952, 2100) and kept in a vacuum-desiccator. Unless specified differently, it was added in the proportion of 1 mole % of monomer.

*cyclo*Hexene (B.D.H.) was stored over calcium chloride and freshly distilled before use; it had b. p. 83·4°, n_D^{18} 1·4472. After reaction, the product was washed with water, to remove catalyst residues, dried ($CaCl_2$), and distilled under reduced pressure. The residue consisted of a yellow oil representing about 1% of the monomer used.

trans-Stilbene (B.D.H.), recrystallised three times from absolute alcohol, and dried under vacuum, had m. p. 125°. Stilbene (2 g.) was dissolved in pure toluene (25 ml.) together with the catalyst, and reaction allowed to proceed under pressure. After evaporation of the toluene at room temperature (heating tended to cause some decomposition), the residue consisted of crystals of stilbene with traces of a viscous oil, n_D^{21} 1·4860 (n_D^{20} for *cis*- and *trans*-stilbene, 1·61 and 1·63—1·68, respectively).

Indene (B.D.H.), fractionated through a glass-packed column, had b. p. 183°, n_D^{25} 1·5650. After reaction, in every case, the solution had darkened slightly. The percentage polymerisation was estimated from the change in refractive index, Breitenbach and Bremer's data (*loc. cit.*) being used; $n_D^{19\cdot5}$ 1·5700 for indene + 1% of catalyst; 1·5805 and 1·6020 for the 5100- and 10,000-atm. fractions respectively.

Polyindene was isolated as a white powder by precipitation with methanol from a solution of the reaction products in ether. This powder, consisting of polymers of very different

molecular weights, was further separated by fractional precipitation with ethanol from a solution in benzene. The physical properties of the resulting polyindene fractions are shown in Table 1.

TABLE 1. *Physical properties of polyindene fractions.*

Fraction	Melting range	Viscosity (sec.) *	*M*
5100 atm., No. 1	230—235°	155	820 †
2	215—225	154	710
3	205—210	151	450
4	(Liquid)	—	Dimers and trimers
10,100 atm., No. 1	210—220	155	820
2	205—210	153	620
3	(Liquid)	—	Tetramers and below

* Time of flow in sec. for a 1% solution in benzene, pure benzene requiring 145 sec.
† 797 cryoscopically in benzene.

The values of the molecular weights were obtained by extrapolation on a melting point–molecular weight curve drawn from the results of Whitby and Katz (*loc. cit.*).

Maleic anhydride (B.D.H.), purified by distillation, and recrystallised from chloroform had b. p. 196°; 4 g. of maleic anhydride + 1 mole % of benzoyl peroxide were dissolved in 25 ml. of pure toluene and allowed to react under pressure. The product, an insoluble, sticky, yellowish solid, was dissolved in acetone, and the solvent evaporated under reduced pressure. The residue was a hard brown solid which charred when heated. Several experiments under the same conditions did not give good agreement, the yield varying from 50 to 70%. The highest value of the molecular weight (determined cryoscopically in water, since the product was insoluble in benzene) was 154.

Diethyl maleate (B.D.H.) was distilled under reduced pressure, and the fraction of b. p. 108°/17mm., n_D^{19} 1·4398, was used. The reaction products were washed with water and dried ($CaCl_2$). After distillation under reduced pressure, the residue, an oil which tended to char when heated, represented about 10% yield.

Diethyl fumarate (B.D.H.), purified in the same way as the maleate, had b. p. 98°/14 mm., $n_D^{19\cdot5}$ 1·4411. At 2000 atm. the product was a viscous oil, which was dissolved in ether, washed with water, and dried. Evaporation under reduced pressure left two fractions, the first (n_D^{20} 1·4595) readily soluble in ether, and the other (n_D^{20} 1·4790) soluble in benzene.

At higher pressures, the product was a transparent solid which softened at 100° and finally melted at about 360°. The polymer was soluble in benzene, acetone, ethanol, and pyridine.

1 : 2-Dibromoethylene (B.D.H.), dried ($CaCl_2$) and freshly distilled before use, had b. p. 110°, n_D^{20} 1·5418. After reaction, the liquid product was brown. It was dissolved in ether, washed with water, and dried. On distillation under reduced pressure, there remained a few drops of an oil, amounting to 2—3% yield.

Methyl cinnamate (B.D.H.), fractionated under reduced pressure, had b. p. 127°/13·5 mm. Because it was suspected that the monomer (m. p. 33°/1 atm.) solidified under pressure, the reaction was carried out in ethanol. The product was a white powder which was filtered off, washed with alcohol, and dried *in vacuo*. The polymer was fairly soluble in benzene and in boiling pyridine. It represented 9% polymerisation. It remained unchanged up to 360°, and was not heated further.

Ethyl cinnamate (B.D.H.), dried ($CaCl_2$) and distilled under reduced pressure, had b. p. 140°/14 mm., n_D^{19} 1·5590. After reaction, the contents of the reaction vessel had become a tough opalescent solid. The polymer was soluble in benzene and boiling chloroform, and to some extent in boiling ethanol. It softened at about 100° and tended to crumble as the temperature was raised to 290°. At 340°, it became brittle.

n-Butyl cinnamate, prepared from cinnamic acid (Jeffery and Vogel, *J.*, 1948, 658), was distilled under reduced pressure; it had b. p. 159°/15 mm., n_D^{20} 1·5400. After reaction under pressure, the product was a transparent solid, which was soluble in benzene, and to a smaller extent in ethanol. Its behaviour, when heated, was similar to that of ethyl cinnamate.

tert.-Butyl cinnamate, prepared from the acid chloride and *tert.*-butyl alcohol (Abramovitch, Shivers, Hudson, and Hauser, *J. Amer. Chem. Soc.*, 1943, 65, 986; *Org. Synth.*, 1944, 24, 19), a yellow oil, was distilled under reduced pressure; it had b. p. 160°/14 mm., n_D^{16} 1·5414 (Found : C, 76·15; H, 8·0. Calc. for $C_{13}H_{14}O_2$: C, 76·4; H, 7·9%). After reaction under pressure, the product was a transparent yellow solid similar in appearance to, but rather softer than,

poly-(*n*-butyl cinnamate). Some traces of unchanged monomer could be discerned between the polymer surface and the Pyrex tube. Heating produced the same reaction as with the ethyl and the *n*-butyl polyester.

Methyl *α-tert.*-butylacrylate (I.C.I. specially purified, n_D^{20} 1·4272), without further treatment, was treated under pressure with 6·2 mols. % of benzoyl peroxide. The products, which were liquid, were taken up with ether and distilled at 11 mm. The monomer distilled over at 28°, leaving a stiff translucent jelly, which remained unaltered for 1 hr. at 100°/11 mm. (n_D^{20} 1·4840). The amount, corrected for catalyst residues, represented 19% of polymerisation. A further sample of monomer was treated with 6·2 mols. % of benzoyl peroxide with the further addition of 0·5 mol. % of *tert.*-butyl perbenzoate as extra catalyst. After similar treatment to the previous sample, a clear transparent viscous liquid remained (n_D^{20} 1·4720), corresponding to 66% of the original sample.

Determination of Molecular Weights.—The molecular weights of polymers were measured in three ways (cf. col. 9 of Table 2).

Cryoscopic method (*C*). The so-called " Beckmann method " was used, the apparatus being the same as that described by Skau and Wakeman (Weissberger, " Physical Methods of Organic Chemistry," Interscience Publ., 1949, Vol. 1, p. 93). B.D.H. " Molecular-weight " benzene was the solvent. Before use, it was further dried by storage over calcium chloride for several weeks, during which the m. p. gradually rose, and finally attained a constant value. This was then taken as the correct m. p.

TABLE 2. *Reaction conditions and polymerisation products.*

	Reaction conditions.				Reaction products.			
1.	2.	3.	4.	5.	6.	7.	8.	9.
Substance	Catalyst *	Temp.	Press. (atm.)	Time (hr.)	Yield (%)	*M*	Order	Method
*cyclo*Hexene	—	60°	3300	22	<1	—	—	—
,, ...	—	90	3400	22	<1	—	—	—
,, ...	*	60	3700	21	1	—	—	—
,, ...	*	90	3700	21	1	—	—	—
Stilbene (S)	*	90	5000	24	—	—	—	—
Indene (1)	—	20	9000	24	some	—	—	—
,, (2)	—	20	12,000	72	10	—	—	—
,, ...	*	90	5100	23	17	850	7	(C & V)
,, ...	*	90	10,100	23	50	850	7	(C & V)
Maleic anhydride (S)	*	60	4900	23	15—20	150	1—2	(C)
,, (S)	*	90	4900	24	50—70	154	1—2	(C)
Diethyl maleate	—	90	4200	18	2	—	—	—
,, ...	*	60	1800	23	6	—	—	—
,, ...	*	60	1800	22	10	—	—	—
Diethyl fumarate ...	*	60	2000	22	60	381—738	2—4	(C)
,, (3)	*	59	2000	22·5	92·5	—	—	—
,, ...	*	60	5000	23	98	1000	6	(C)
,, ...	*	57	10,000	24	~100	1530	9	(C & V)
Methyl cinnamate (S)	*	60	5000	23	9	4000	24	(O)
Ethyl cinnamate (4)	—	125	4000	240	58·5	—	—	—
,, ...	*	100	5000	23	99	4900	27	(O)
n-Butyl cinnamate...	*	90	4400	22	98	6100	29	(O)
tert.-Butyl cinnamate	*	90	4400	22	90	3800	18	(O)
1 : 2-Dibromoethylene	*	80	5300	23	1	—	—	—
,,	*	90	5100	47	2—3	—	—	—
,,	*	100	10,000	23	3	—	—	—
Methyl α-*tert.*-butyl acrylate	†	100	10,000	23	19	230	1—2	(C)
,,	† + (5)	130	10,000	23	66	320	2—3	(C)

* The asterisk in col. 2 denotes 1 mol. % of benzoyl peroxide; † denotes 6·2 mols. % of benzoyl peroxide. (S) Indicates that the reaction was carried out in a solvent. (1) and (2) Results reported by Bridgman. (3) Results reported by Starkweather. (4) Results reported by Newitt *et al.* (5) Additional catalyst was 0·5% of *tert.*-butyl perbenzoate.

Viscosity method (*V*). The instrument used throughout was an Ostwald No. 1 capillary viscometer. While readings were taken the instrument was immersed in a thermostat at 20°. The time of flow was the mean of at least three runs. In calculating the molecular weights from the viscosity data the simple Staudinger relation $[\eta] = KM$ was used in view of the comparatively low order of molecular weights.

Osmotic pressure method (*O*). These measurements were carried out in the Chemical Research Laboratory, Teddington. A polyvinyl alcohol semipermeable membrane was found to be the most suitable. Details of the process are similar to those reported by Hookway and Townsend (*J.*, 1952, 3190).

Discussion

As Table 2 shows, although some of the compounds do not react to any significant extent or give products of very low molecular weight, the polymerisation of the others is favoured by high pressure. Higher yields of polymer are obtained in much shorter times than those recorded at normal pressures, as is well shown by, *e.g.*, methyl and ethyl cinnamate. There is also an increased degree of polymerisation. The polymer from diethyl fumarate at 5000 atm. contains six units, and at 10,000 atm. nine units. Polyindene, however, contains seven units whether it is formed at 5100 or 10,000 atm. These broad findings accord with previously reported effects of pressure on the polymerisation of other types of substituted ethylenes.

More than one mechanism may be operative in each stage of a radical-chain polymerisation. Thus chain termination may take place by mutual combination of two radicals, disproportionation between two radicals, chain transfer to monomer, or chain transfer to polymer. Where a solvent is used, there may also be interaction between radicals and solvent molecules. The observed effects of pressure may, therefore, be explained in a number of different ways, involving retardation or acceleration of the various stages. Merrett and Norrish (*Proc. Roy. Soc.*, 1951, *A*, **206**, 309), in the only detailed study of an individual polymerisation at high pressure so far published, found that the chain propagation was accelerated about 10-fold at 60°/5000 atm., while the initiation reaction rate was hardly affected.

It is probable that acceleration of the propagation stage occurs in those of the nine reactions responsive to pressure which yield polymers. Acceleration of organic reactions by pressure is generally found when the formation of the transition state is accompanied by a local decrease in volume. There is also evidence that pressure may overcome some degree of steric hindrance when this is not sufficient to prevent the reaction completely at ordinary pressure (Weale, *J.*, 1954, 2959). An acceleration of propagation relative to termination by the chain-transfer mechanism is qualitatively understandable, as the bimolecular addition of growing polymer to monomer will proceed through a more compact transition state than a reaction in which bond-lengthening is involved.

The monomers studied may be grouped into the three categories: (*a*) symmetrical olefins, *viz.*, stilbene, 1 : 2-dibromoethylene, maleic anhydride, diethyl maleate, and diethyl fumarate; (*b*) asymmetrical olefins, which include the cinnamic esters and methyl α-*tert.*-butylacrylate; (*c*) the homocyclic olefins *cyclo*hexene and indene.

(*a*) The symmetrical olefins include two of the three most resistant to polymerisation. 1 : 2-Dibromoethylene hardly reacts at all even at 10,000 atm., although 1 : 2-dichloroethylene polymerises quite readily at this pressure (*idem*, *J.*, 1952, 2223). This result illustrates the inability of hydrostatic pressure to overcome a high degree of steric hindrance. A model of the chloro-substituted polymer was strain-free, but, owing to the greater size of the bromine atoms, a model of the bromo-polymer could not be made without a large amount of strain.

The two esters and maleic anhydride all reacted; the failure to obtain a product of high molecular weight from the latter may be due to the use of a solvent for this reaction. In these instances, steric hindrance probably does not influence the reaction rates. The greater reactivity of the fumarate than of the maleate has been observed in copolymerisations at ordinary pressure (Lewis, Walling, Cummings, Briggs, and Mayo, *J. Amer. Chem. Soc.*, 1948, **70**, 1519; Doak, *ibid.*, p. 1525; Mayo, Lewis, and Walling, *ibid.*, p. 1529; Lewis and Mayo, *ibid.*, p. 1533; Walling, Seymour, and Wolfstirn, *ibid.*, p. 1544). Lewis and Mayo attribute this to the fact that the fumarate but not the maleate may assume a configuration in which the carbonyl and olefin groups are coplanar, so facilitating resonance-stabilisation of the free radical. As would be expected, this difference persists at high pressures.

The lack of reactivity of stilbene is also not due to steric hindrance, and the ethylenic carbon atoms resemble in inertness those of *cyclo*hexene, which is discussed below.

(*b*) Among the asymmetrical olefins, the four esters of cinnamic acid were all polymerisable much more readily than Marvel and McCain (*loc. cit.*) found at ordinary pressure. The rather low yield from methyl cinnamate is probably due to interference by solvent in the initiation stage, as the order of polymerisation compares with that of the ethyl ester. In these compounds, the resonance stabilisation of the radicals (conjugation of the benzene nucleus with the double bond) is unlikely to be affected by the ester group, and the contribution of the latter should depend almost entirely on its steric effect. The order of the polymers is very similar as far as *n*-butyl, which is probably sufficiently flexible for there to be no hindrance to propagation. The polymer from *tert.*-butyl cinnamate is, however, of definitely lower order, and models indicate a considerable degree of steric strain in this reaction. In view of the excellent yield of polymer, this may well be an example of high hydrostatic pressure overcoming steric hindrance.

The yield from methyl α-*tert.*-butylacrylate is also increased at 10,000 atm. over that obtained by Crawford (*loc. cit.*) at 1 atm. The order of the polymer, however, remains low, and the steric hindrance which Crawford found to oppose head-to-tail propagation (but not head-to-head dimerisation) is presumably too great to be much affected by compression of the reacting system.

(*c*) Of the two homocyclic olefins examined, indene was found to polymerise as previously reported, but the yield from *cyclo*hexene was very low. These reactions are unhindered, and the low reactivity of *cyclo*hexene (which tends to disappear at high temperature and pressures, according to Vereshchagin *et al.*, *loc. cit.*) cannot be ascribed to this cause.

Relation of Polymerisability to the Index of Free Valence.—In radical polymerisation the free radical in attacking the monomer seeks an unpaired electron. Thus the energy required to localise one unpaired electron at a particular carbon atom of the monomer is a measure of the compound's readiness to under go a free-radical chain-reaction (Wheland, *J. Amer. Chem. Soc.*, 1942, **64**, 900; Coulson, *Research*, 1951, **4**, 307). On a particular atom the concentration of electrons not engaged in bonding, and therefore available for reaction, is known as the index of free valence. This quantity has been calculated in a number of cases, and some success has been achieved in establishing a relationship between the free valence and the reactivity towards free radicals (Roitt and Waters, *J.*, 1952, 2695; Kooyman and Farenhorst, *Nature*, 1952, **169**, 153; Kerichi Fukui, Teijiro Yonezawa, Chikayoshi Nagata, and Haruo Shangu, *J. Chem. Phys.*, 1954, **22**, 1433). Therefore information about radical polymerisation might be obtained by studying the free valences of the carbon atoms at both ends of the double bond in the compounds mentioned above.

TABLE 3.

1. Substance	2. C atoms	3. Free valence	Ref.*	5. Free valence	6. Frontier electron density	7. Bound valence
Benzene	all	0·40	*a*	0·40	—	2·000
		0·347	*b*			
*cyclo*Hexene	1 & 2	—	—	0·952	—	—
Naphthalene	α	0·489	*c*	0·427	0·362	1·875
		0·40	*b*			
	β	0·452	*c*	0·390	0·138	2·015
Indene	1	0·372	*d*	0·424	—	—
	2	0·616	*d*	0·668	—	—
Stilbene	α	0·481	*c*	0·497	0·340	1·882
Styrene	α	0·415	*c*	0·547	0·259	1·927
	β	0·821	*c*	0·907	0·683	1·619

* *a*, Coulson, "Valence," Oxford, 1952, p. 254. *b*, Kooyman and Farenhorst, *Nature*, 1952, **169**, 153. *c*, Vroelant, *Compt. rend.*, 1952, **235**, 958. *d*, Pullman and Berthier, *Bull. Soc. chim. France*, 1948, 551.

In Table 3 the values of the index of free valence taken from a number of sources are recorded in col. 3. These values were calculated by using bond-length data from the

following sources: stilbene (Robertson and Woodward, *Proc. Roy. Soc.*, 1937, *A*, **162**, 568), styrene (Penney and Kynch, *ibid.*, 1938, *A*, **164**, 409), naphthalene (Abrahams, Robertson, and White, *Acta Cryst.*, 1939, **2**, 233), indene (Pullman and Bertier, *Bull. Soc. chim. France*, 1948, 551), and benzene (Coulson, *op. cit.*, pp. 253, 254). See col. 5.

Frontier electron densities, quantities calculated by Kerichi Fukui *et al.* (*loc. cit.*), which are similar to the free valence, are shown in col. 6.

The " bound valence," which is complementary to the free valence (Ruedenberg and Sherr, *J. Chem. Phys.*, 1953, **21**, 1565; Sherr, *ibid.*, p. 1582), is included in col. 7.

In the case of *cyclo*hexene there are no reliable data for the bond lengths. Some workers have assumed the values 1·35 Å and 1·54 Å for the C=C and the C–C bond, respectively (Beckett, Freeman, and Pitzer, *J. Amer. Chem. Soc.*, 1948, **70**, 4227; Lister, *ibid.*, 1941, **63**, 143). These figures lead to the high value of 0·932 for the free valence. It seems, however, unlikely that the double bond and the two adjacent single bonds do not undergo some sharing of order. Indeed, the values of the ionisation potential for benzene (9·52 and 9·45 ev) and *cyclo*hexene (9·24 ev) (Morrison and Nicholson, *J. Chem. Phys.*, 1952, **20**, 1021) suggest that the double-bond order is not very different from that of benzene, with the remaining bonds becoming progressively more single in character. As for the other values in the Table, it is clear that, although there are differences due to the method of calculation, the general agreement is very good.

From these results it is seen that both styrene and indene, which polymerise readily, have a high free valence at one end of the double bond. A free radical can attach itself at that point, and the resulting complex is another free radical with a high free valence at the second carbon atom.

In the case of stilbene the free valence is small on both the carbon atoms, and such a reaction cannot easily take place. Benzene, however, has also a small free valence, but is subject to attack by benzoyl peroxide (Gelissen and Hermans, *Ber.*, 1925, **58**, 285). It is probable that the symmetry of the ring allows the excess of electron density to be shared among the remaining carbon atom sites.

*cyclo*Hexene is not easily explained. However, the considerable strain in the ring structure will probably go towards neutralising the effect of the apparent high free valence. This is supported by the fact that at high temperatures, *i.e.*, with sufficient energy input, the molecule will readily undergo catalysed polymerisation (Zelinskii and Vereshchagin, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1945, **44**; Nemtzov, Nizokina, and Soskina, *J. Gen. Chem. U.S.S.R.*, 1938, **8**, 1303).

Because reliable data are only available for a few compounds, the evidence is not complete. However, it seems reasonable that polymerisability of these hydrocarbons when steric hindrance is absent may be related to the size of the free valence on the carbon atoms of the " active " double bond.

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The Polarized Spectrum of Anthracene. Part II. Weak Transitions and Second-order Crystal Field Perturbations.*

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Forces between molecules in aromatic crystals are small compared with intramolecular forces, allowing the energy levels and spectral intensities in crystals to be treated by perturbation methods. In intense molecular transitions the most important effect of a monoclinic crystal field is "Davydov" splitting of the upper state into two components giving two crystal absorptions, one polarized parallel and the other perpendicular to the *b* crystal axis. The Davydov splitting is proportional to the intensity and, in transitions of low intensity, it is not the only important effect, for the upper state of the weak transition in one molecule interacts with the upper states of strong transitions in neighbouring molecules to cause changes comparable to and perhaps exceeding it. These second-order perturbations alter the splitting and may upset the oriented-gas intensity ratios, especially if a weak and a strong band system are close together.

If vibrational sublevels share the intensity of a system each behaves as a separate upper state and has distinct values of splitting and intensity ratio. This leads to irregularities in progression spacings which, like the other effects, are characteristic of the properties of the parent, isolated molecule, excited states and may be used to identify them.

The theory of these effects is applied to anthracene with various assumptions. Values are calculated for band splittings and intensities in the 3800-Å system.

In the strong anthracene absorption near 2500 Å (Part I, *J.*, 1955, 539) the dominant effect of the crystal field is a resonance splitting of the double degeneracy due to the presence in the unit cell of two molecules with identical energy levels. The theory of this type of splitting was first studied by Davydov (*Zhur. eksp. teor. Fiz.*, **1948**, **18**, 210); it is properly called a first-order crystal field perturbation because its size is approximately calculable by first-order perturbation theory applied to wave functions of the isolated molecules. The splitting is proportional to the square of the transition moment, and in the intense transitions commonly found in aromatic molecules (*e.g.*, naphthalene 2200 Å, anthracene 2500 Å, tetracene 3000 Å) it may amount to some thousands of wave numbers, corresponding to transition moments of about 3 Å. Conditions in weak transitions are very different and we discuss in this Part the effect of crystal forces in the long-wave aromatic systems of intensity of about $f = 0{\cdot}1$. The Davydov splitting is a few hundreds of wave numbers at most and may be much less; we shall show that second-order effects are comparable, especially where there is a strong transition near the weak one. Moreover, under these conditions the oriented-gas intensity ratios are seriously wrong: the upper states of separate free molecule transitions become mixed by crystal forces resulting in intensity transfers between weak transitions and stronger ones, with a superficial resemblance to the well-known Herzberg–Teller intensity-stealing by vibrational perturbations. The following discussion deals with second-order crystal field perturbations with special reference to the 3800-Å anthracene system which will be analyzed and assigned in Part III (following paper); it falls into two parts: (i) energy changes due to interactions between crystal wave functions based on different molecular-state wave functions, and (ii) intensity transfers between perturbed molecular transitions.

The notation used in Part I must now be adapted to describe several molecular excited states instead of one only. Superscripts attached to wave functions and energies as in the molecular wave functions φ^r, their energies w^r, and the crystal functions Φ^r, refer to an upward energy sequence of molecular excited states; subscripts are used throughout as a means of distinguishing different molecules.

* Part I, *J.*, 1955, 539.

Second-order Energy Terms.—According to the analysis given in Part I each excited molecular state of anthracene splits into two manifolds of crystal levels all with the same parity as the molecular state but transforming in other respects like different representations of the unit cell group C_{2h}. Table 1 of Part I (*loc. cit.*) gives the symmetries of the associated crystal and molecular states. One finds, for example, that a B_{2u} molecular state has a B_u crystal component (*ac* polarized) and an A_u component (*b* polarized). To a good approximation, optical transitions are allowed only to that one level of each manifold with zero values of the wave vectors k_a, k_b, and k_c [Part I, Equation (14) *et seq.*] and in this case each band in the vapour spectrum splits into two spectral lines in the crystal (Part I, Fig. 2). These lines record transitions from the crystal ground state to two upper states, described approximately as products of molecule functions φ and φ^r for the ground and r-th excited state. We write for the first excited state ($r = 1$),

$$\phi_l{}^1 = \varphi_1\varphi_2 \ldots \varphi_l{}^1 \ldots \varphi_N \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and, by combining the product functions ϕ according to representations of the unit cell group,

$$\left.\begin{aligned}\gamma^{1\alpha} &= (1/\sqrt{2})(\phi_1{}^1 + \phi_2{}^1)\\ \gamma^{1\beta} &= (1/\sqrt{2})(\phi_1{}^1 - \phi_2{}^1)\end{aligned}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where the subscripts number the two molecules of one unit cell. The symmetry properties of γ depend on the symmetry of φ and φ^1 in (1); in the case of most interest, where φ^1 is either of species B_{2u} or B_{3u} of D_{2h}, $\gamma^{1\alpha}$ transforms like B_u of C_{2h} and $\gamma^{1\beta}$ like A_u.

The zero wave-vector crystal wave functions are

$$\Phi^{1\alpha,1\beta} = (1/\sqrt{N/2}) \sum_{\mu,\nu,\omega} \gamma^{1\alpha,1\beta}\,(\mu, \nu, \omega) \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where the summation is over all the unit cells with co-ordinates (μ, ν, ω). The first-order splitting between $\Phi^{1\alpha}$ and $\Phi^{1\beta}$ is, from Part I, equation (17): $2\sum_m I_{lm}{}^1$ where

$$I_{lm}{}^1 = \int \varphi_l{}^1\varphi_l{}^1 \mathbf{V}_{lm}\varphi_m\varphi_m{}^1 \, d\tau$$

$\mathbf{V}_{lm}$ is the intermolecular potential [Part I, equation (1)] and m runs over molecules not translationally equivalent to l.

According to (2) we derive from each molecular excited state φ^r two unit cell functions $\gamma^{r\alpha}$ and $\gamma^{r\beta}$ from which crystal wave functions (3) may be built. The first-order zero wave-vector crystal wave functions are formed by linear combination of the unperturbed functions (3) based on all the excited states r of the same parity with coefficients chosen to minimize the intermolecular energy. Proceeding conventionally we find that the excitation energy of the desired zero wave-vector crystal state is given by the lowest eigenvalue of an energy matrix of which the diagonal elements H^{rr} have the form of equation (17) of Part I, namely, for species B_u,

$$H^{rr} = \Delta w^r + D^r + \sum_p{}' I_{lp}{}^r + \sum_m{}' I_{lm}{}^r \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

in which, as usual, the subscript p refers to molecules translationally equivalent to l, and m to the others. The non-diagonal elements H^{rs} are composed of integrals J and K, connecting two different molecular transitions:

$$H^{rs} = \sum_p{}' K_{lp}{}^{rs} + \sum_m K_{lm}{}^{rs} + \sum_p{}' J_{lp}{}^{rs} + \sum_m J_{lm}{}^{rs} \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$\left.\begin{aligned}K_{lp}{}^{rs} &= \int \varphi_l{}^r\varphi_l{}^s \mathbf{V}_{lp}\varphi_p\varphi_p \, d\tau\\ J_{lp}{}^{rs} &= \tfrac{1}{2}\left(\int \varphi_l\varphi_l{}^s \mathbf{V}_{lp}\varphi_p\varphi_p{}^r \, d\tau + \int \varphi_l\varphi_l{}^r \mathbf{V}_{lp}\varphi_p\varphi_p{}^s \, d\tau\right)\end{aligned}\right\} \quad . \quad . \quad . \quad . \quad (6)$$

$\varphi_p{}^s$ being the wave function for the p-th molecule in its s-th excited state. Expression (5), like (4), belongs to the B_u matrix; the elements of the A_u matrix are obtained by changing the signs of the last term in (4) and in (5).

The integrals K vanish in the dipole approximation; however, although small, they are

of some interest and are discussed at the end of this section. The integrals J may be evaluated as described in Part I. Expanding $\mathbf{V}_{lp}$ and retaining only the dipole–dipole term, we find (cf. I.15)

$$J_{lp}^{rs} = \tfrac{1}{2}(-e^2/r_{lp}^3)|\boldsymbol{M}^r||\boldsymbol{M}^s|\Big\{2\cos\theta_{l1}^r\cos\theta_{p1}^s + 2\cos\theta_{l1}^s\cos\theta_{p1}^r - \cos\theta_{l2}^r\cos\theta_{p2}^s - \cos\theta_{l2}^s\cos\theta_{p2}^r - \cos\theta_{l3}^s\cos\theta_{p3}^r - \cos\theta_{l3}^r\cos\theta_{p3}^s\Big\} \quad . \quad . \quad (7)$$

where r_{lp} is the distance between the l-th and p-th molecules and θ_{l1}^s, for example, is the angle between the transition moment for the s-th excited state of the l-th molecule and the line joining the centres of the l-th and p-th molecules. If the transitions to states s and r have the same polarizations, the numerical factors in the integrals are the same as quoted in Table 3 of Part I. Table 1 summarizes all the values to the dipole–dipole approximation including neighbouring molecules up to 20 Å separation in the crystal. For $r = s$ one has $J_{lp}^{rr} = I_{lp}^{r}$.

TABLE 1. *Intermolecular integral sums for anthracene* (cm.$^{-1}$ Å^{-2}).

	Both transitions $A_g - B_{3u}$	Both transitions $A_g - B_{2u}$	Mixed polarizations $A_g - B_{3u}$ and $A_g - B_{2u}$
$\sum_p J_{lp}^{rs}/\|\boldsymbol{M}^r\|\|\boldsymbol{M}^s\|$	−990	728	292
$\sum_m J_{lm}^{rs}/\|\boldsymbol{M}^r\|\|\boldsymbol{M}^s\|$	96	1532	1284

If the perturbation conditions $H^{rr} - H^{11} \gg H^{r1}$ hold we may write the excitation energy of the lowest excited crystal state in the second-order perturbation form:

$$\Delta E = H^{11} + \sum_r{}'(H^{1r})^2/(H^{11} - H^{rr}) \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

The labour of diagonalizing the energy matrix rigorously is not justified unless the inequality above is seriously disobeyed.

The quantities in Table 1, appropriately multiplied by the experimental transition moments, and taken together with the vapour excitation energies Δw allow all the quantities appearing on the right hand side of (8) to be calculated with the exception of the K's, which are small, and of the D^r defined in equation (8) of Part I. It will be observed that where D^r occurs in (4) it does so in the same way for A_u and B_u states. If therefore we disregard the absolute excitation energies and calculate the splittings $\Delta E(B_u) - \Delta E(A_u)$ the quantities D^r will cancel from the first-order terms and appear only in the denominator in the second-order terms, and there as differences $(D^r - D^s)$; moreover the denominator also contains the difference $(\Delta w^r - \Delta w^s)$ which will in most cases be much the larger term. This suggests that we might reasonably ignore differences between the D integrals and set $(D^r - D^s) = 0$ throughout; alternatively the denominators in (8) might be taken directly from the observed spacings in the crystal spectrum. This latter has been adopted in the calculations reported on p. 2307.

Crystal Field Effect on Intensities.—Crystal forces mix the crystal wave functions for different molecular states, and the transition intensities of the molecular spectrum are consequently redistributed in the crystal spectrum. The extent of this redistribution differs in the two crystal directions and so alters the intensity ratio from the oriented-gas value. To calculate magnitudes we start from the wave functions corrected to the first order. Aside from a normalizing multiplier very near to unity, these are

$$\Psi^1 = \Phi^1 + \Big\{H^{12}/(H^{11} - H^{22})\Big\}\Phi^2 + \ldots + \Big\{H^{1r}/(H^{11} - H^{rr})\Big\}\Phi^r + \ldots \quad . \quad (9)$$

in which the zero-order functions Φ^1 etc. are all of the same crystal symmetry species. The transition moment per unit cell from the ground state to Ψ^1 may be expressed in terms of the free molecule moments $\boldsymbol{M}_1^r$ and $\boldsymbol{M}_2^r$ for the two molecules in the unit cell, as in (10). The upper signs refer to the B_u, *ac* polarized species, and the lower to the A_u, *b* polarized species.

$$\mathcal{M}^{\alpha,\beta} = (1/\sqrt{2})\Big[(\boldsymbol{M}_1^1 \pm \boldsymbol{M}_2^1) + \sum_r{}'\Big\{H^{1r}/(H^{11} - H^{rr})\Big\}(\boldsymbol{M}_1^r \pm \boldsymbol{M}_2^r)\Big] \quad . \quad (10)$$

The experimental intensities to be reported and discussed in Part III may be related to the oscillator strength f of the molecular transition, which may in turn be related to the theoretically determined transition moment:

$$f = A \,.\, \Delta E \,.\, Q^2;\; eQ = \mathscr{M}/\sqrt{2} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

where A is a geometrical factor depending on the inclination of $\mathscr{M}$ to the molecular and crystal axes; ΔE, the transition energy, is measured in Rydbergs and Q, the dipole length, in atomic units. The ratio of oscillator strengths for absorption polarized along the two crystal axes is the *polarization ratio*. If the small difference in ΔE for the a and b crystal transitions is ignored the polarization ratio is given as the ratio of the calculated quantities (12). This may be compared with the oriented-gas value (13) from which it differs by the presence of the first-order terms in equation (10):

$$\left\{\mathscr{M}^{\alpha} \,.\, \mathbf{a}/|\mathscr{M}^{\beta}|\right\}^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

$$\left\{(\mathbf{M}_1^{1} + \mathbf{M}_2^{1}) \,.\, \mathbf{a}/|(\mathbf{M}_1^{1} - \mathbf{M}_2^{1})|\right\}^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

where $\mathbf{a}$ is a unit vector along the a crystal axis.

Quantitative examples of the application of formulæ (10) and (12) will be given later. We now consider some qualitative features of the crystal-induced intensity transfer. The meaning of the formulæ is clearer if there are just two transitions concerned, one weak and one strong. In the crystal each of these splits into ac and b polarized components which behave independently. According to (10) a fraction of the oriented-gas transition moment of the $ac(b)$ component of the stronger transition is compounded with the $ac(b)$ component of the weaker. If the matrix element H^{12} is positive and the crystal transition moments have the same sign the weak transition is strengthened; under other conditions it may be weakened. The magnitude of the transfer is greatest when the intense system has a large $ac(b)$ component and H^{12} is large. Now H^{12} is itself a function of the molecular transition moments $\mathbf{M}^1$ and $\mathbf{M}^2$; we find that if the weak transition is very weak H^{12} is so small that transfer is negligible, on the other hand if the "weak" transition is in fact of comparable intensity with the strong the transferred transition moment is small compared with the transition moment already present and its effect is *relatively* small. In general, transfer should be most noticeable when the weak system is say 0·1 — 0·2 times as strong as the intense one, and greatest in the crystal direction in which the strong transition has its major component, *i.e.* in the ac plane for an $A_g - B_{3u}$ system and along b for an $A_g - B_{2u}$. It follows from this last consideration that the transfer in the a and b directions will usually be very different, and therefore that the polarization ratio (12) will depart considerably from the oriented gas value.

We must now return to a consideration of the integrals K in (5), hitherto neglected. Like the terms in D^r these integrals vanish in the dipole approximation but their consideration cannot be avoided in the same way, *i.e.* by regarding the denominator in (8), in which the D^r occur, as an empirical parameter. It is necessary to form an estimate of the size of the K integrals and then to discuss their significance. The first contribution to the integral K_{lp}^{rs} in the expansion of $\mathbf{V}_{lp}$ is the interaction between the static quadrupole moment of one molecule in its ground state with the transition quadrupole moment of another molecule for transitions between its r-th and s-th states. The practical upper limit to the product of components of the two moments is about 1 Å^4, leading to interaction terms about $(1/r_{lp})^3$ times the dipole terms, or about 1/25 for the nearest neighbours which provide the only significant terms. One arrives in this way at an upper limit to the sum of the K integrals of about 1/25 times the greatest of the J sums in Table 1, that is (1/25) × (728 + 1532) cm.$^{-1}$, giving 90 cm.$^{-1}$. Now it is easily verified that addition of a term of this size to H^{1r} in (8) for both A_u and B_u states makes a negligibly small difference to the splitting so long as the dipole moment product exceeds 0·2, a limit which is well below the actual value. This justifies our neglect of the K integrals in the calculations described on p. 2306 and 2307.

Having discussed the effect of a monoclinic crystal field in a strong transition (Part I)

and in a transition of medium intensity we now consider briefly the case of very weak transitions in which, as will be seen, the K integrals are quite important. In a band system as weak as the benzene 2600-Å or naphthalene 3200-Å systems the transition moment amounts to a few hundredths of an Å at most, so that even if the strong perturbing transition has a moment of 2 or 3 Å the product $|\boldsymbol{M}^r||\boldsymbol{M}^s|$ is probably not more than 0·10. Evidently the second-order splitting at its greatest is less than 5 cm.$^{-1}$, and the first-order negligible; intensity transfer will be correspondingly small. The integrals K contributing to H^{rs} are independent of the transition dipole moments, and so under these conditions could be comparable to the dipole-dependent integrals J. This amounts to saying that, in very weak systems, the intermolecular *resonance* effects (splitting and intensity transfer) die out and one is left with a feeble van der Waals type of interaction. This gives no splitting, since the K-dependent part of H^{rs} is the same for A_u and B_u states, and its effect on intensities is intramolecular, *i.e.*, it causes a mixing of states of the same parity in one molecule. Naturally the selection rule for the mixing depends on the symmetry of the crystal field: in the monoclinic fields of aromatic crystals each molecule is at a centre of symmetry, and only states of the same parity are mixed. If we accept the estimate of 90 cm.$^{-1}$ for the K integral sum and suppose the two states eligible for mixing to be 10^4 cm.$^{-1}$ apart, the intensity-borrowing amounts to about 10^{-4} the strong system's intensity, which is comparable to the borrowing caused by vibrational perturbations.

Influence of Vibrational Structure.—Leaving the case in which the intensity of the absorption system is concentrated in one band, we must now deal with the common situation of a band system in which the intensity is spread over several bands to form a progression, or progressions, in one or more vibrations. Each of these sublevels must appear separately in the energy matrix formed from elements (4) and (5). To a good approximation the wave functions for these molecular vibronic states may be written as products $\varphi^r \cdot \sigma^{r(n)}$ of an electronic function and a vibrational function $\sigma^{r(n)}$ appropriate to the n-th quantum state of the vibration appearing in the progression. The vibration will in general differ from one electronic state r to another. For simplicity we shall examine the case in which only one strong progression occurs; in the ground state all molecules will be supposed to be in the zeroth quantum state $\sigma^{0(0)}$ of the active vibration. The ground-state molecular wave function is now $\varphi \cdot \sigma^{0(0)}$ and the upper states are $\varphi^r \cdot \sigma^{r(n)}$ for as many electronic states r as are energetically significant. The integrals I and J are replaced by integrals over vibrational as well as electronic co-ordinates. These may be expressed:

$$J_{lm}^{r(n),s(n')} = \tfrac{1}{2}\left(\int \varphi_l \sigma_l^{0(0)} \varphi_l{}^r \sigma_l^{r(n)} \mathbf{V}_{lm} \varphi_m \sigma_m{}^{0(0)} \varphi_m{}^s \sigma_m{}^{s(n')} \,\mathrm{d}\tau + \int \varphi_l \sigma_l{}^{0(0)} \varphi_l{}^s \sigma_l{}^{s(n')} \mathbf{V}_{lm} \varphi_m \sigma_m{}^{0(0)} \varphi_m{}^r \sigma_m{}^{r(n)} \,\mathrm{d}\tau\right)$$

$$= \xi^{r(n)} \xi^{s(n')} J_{lm}{}^{rs} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

where

$$\xi^{r(n)} = \int \sigma^{0(0)} \sigma^{r(n)} \,\mathrm{d}\tau_{\mathrm{vib.}}$$

The quantities ξ are the well-known Franck–Condon overlap factors. Values of $(\xi^{r(n)})^2$ can be found from vapour and solution absorption spectra, where they are proportional to the intensities of the members of the progression in the vibration σ. In real examples, at any rate in simpler aromatic compounds, two circumstances simplify the problem. There is usually only one very intense transition within easy energy reach of the weaker transition, and in many cases this intense system shows no well-developed progression but has its intensity concentrated in one rather narrow band group. It is quite realistic therefore to simplify the problem to that of a ground state φ, a weakly excited upper state φ^1 with accompanying vibrational sublevels, and an intensely excited upper state φ^2 without vibrational structure. The energy matrix for this problem is equal in order to the total number of vibronic levels of the two upper states. Two new types of matrix element occur. First, for the sublevels of one electronic level:

$$H^{1(n)1(n)} = \Delta w^1 + D^1 + (\xi^{1(n)})^2 \left\{ \sum_p{}' I_{lp}{}^1 + \sum_m I_{lm}{}^1 \right\} \quad . \quad . \quad . \quad . \quad (15)$$

$$H^{1(n)1(m)} = \xi^{1(n)} \xi^{1(m)} \left\{ \sum_p{}' I_{lp}{}^1 + \sum_m I_{lm}{}^1 \right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$

and secondly, joining the two electronic levels:

$$H^{1(n)2(0)} = \xi^{1(n)}\left\{\sum_p{}' J_{1p}{}^{12} + \sum_m J_{1m}{}^{12}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad (17)$$

where the expressions refer to the B_u components. It may happen that the quantities in equation (16) are small compared to the interval $h\nu$ between vibrational sublevels. It is then a good approximation to write for the crystal excitation energy of the n-th sublevel of φ^1 the expression, for the B_u component,

$$H^{1(n)1(n)} + \sum_m{}'(H^{1(n)1(m)})^2/(nh\nu - mh\nu) + (H^{1(n)2(0)})^2/(H^{1(n)1(n)} - H^{22}) \quad . \quad (18)$$

To obtain the corresponding A_u excitation energy it is only necessary to change the signs of the last terms in each of expressions (15), (16), and (17). Since both B_u and A_u energies depend similarly on $\xi^{1(n)}$ the splittings will be roughly proportional to the intensities along the progression and, because $(\xi^{1(n)})^2 < 1$, they will all be smaller than in the hypothetical case of a system in which the same total intensity is concentrated in one band.

To deal with changes in the polarization ratio we consider the transition moments for excitation to the n-th vibrational quantum level of φ^1. In the B_u component

$$\mathscr{M}^{\alpha}(n) = 2^{-\frac{1}{2}}\left\{\xi^{1(n)}(\boldsymbol{M}_1{}^1 + \boldsymbol{M}_2{}^1) + \xi^{1(n)}H^{12}/(H^{1(n)1(n)} - H^{22}) \,.\, (\boldsymbol{M}_1{}^2 + \boldsymbol{M}_2{}^2)\right\} \quad . \quad (19)$$

An analogous expression holds for $\mathscr{M}^{\beta}(n)$. The polarization ratio is evidently independent of the Franck–Condon factors, which cancel, and it changes from member to member of the progression only through the slowly varying energy difference $H^{1(n)1(n)} - H^{22}$. Indeed if variations in this were neglected the polarization ratio would be constant along the progression and equal to the value for a concentrated system. In actual examples however the variation in ratio is not negligible, but it is true that the polarization ratio is much less sensitive to details of the vibrational structure than is the splitting.

Application to Anthracene.—In this section we shall apply the theory to see how second-order crystal perturbations affect the spectrum of anthracene. The intense system, denoted on p. 2306 by φ^2, is now the anthracene absorption at 2500 Å assigned to the species $A_g - B_{3u}$ in Part I. φ^1 is the system at 3800 Å (oscillator strength $f = 0{\cdot}1$) which appears in the vapour in a progression of five or more members with a spacing of 1400 cm.$^{-1}$. Discussion of the measured crystal spectrum and comparison with theory is left to Part III; here we are concerned only with calculating the crystal energy levels and polarization ratios corresponding to the weak vapour system using the theory developed earlier under each of the two plausible assignments for the system. The starting data include the solution intensity distribution along the progression, the relative values of which we equate to the quantities $(\xi^{1(n)})^2$ as follows: $n = 0$: 0·324, $n = 1$: 0·316, $n = 2$: 0·218, $n = 3$: 0·093, $n = 4$: 0·050. The interaction integrals are otherwise determined by the values in Table 1 and by the transition moments $|\boldsymbol{M}^1| = 0{\cdot}61$ Å and $|\boldsymbol{M}^2| = 2{\cdot}3$ Å found in the solution spectrum.

For Table 2 and Fig. 1 it is assumed that the 3800 Å system has the same polarization as the intense system, *i.e.*, belongs to the species $A_g - B_{3u}$. Table 3 and Fig. 2 assume, contrariwise, that the polarization is $A_g - B_{2u}$. In order that the individual terms of the energy may be compared the Tables show separately the splitting calculated with and without the last term of equation (18), which measures the second-order effect of φ^2 on φ^1.

TABLE 2. *Assumption: Weak system assigned* $A_g - B_{3u}$.

n	First-order splitting (cm.$^{-1}$)	B_u component * by (18) (cm.$^{-1}$)	A_u component * by (18) (cm.$^{-1}$)	Splitting by (18) (cm.$^{-1}$)	Polarization ratio a/b
0	300	+71	−146	217	2·3 : 1
1	364	$+h\nu + 142$	$+h\nu - 140$	282	1·9 : 1
2	281	$+2h\nu + 127$	$+2h\nu - 98$	225	1·5 : 1
3	121	$+3h\nu + 55$	$+3h\nu - 44$	99	1·1 : 1
4	50	$+4h\nu + 10$	$+4h\nu - 29$	39	0·7 : 1
Concentrated system	1133	+444	−422	866	2·3 : 1

* Omitting throughout the constant $\Delta w^1 + D^1$.

TABLE 3. *Assumption: Weak system assigned* $A_g - B_{2u}$.

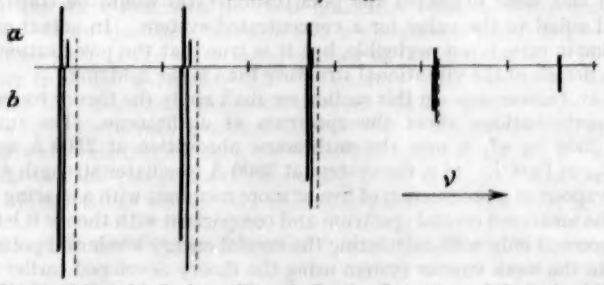
n	First-order splitting (cm.$^{-1}$)	B_u component * by (18) (cm.$^{-1}$)	A_u component * by (18) cm.$^{-1}$)	Splitting by (18) (cm.$^{-1}$)	Polarization ratio a/b
0	28	-180	-209	29	1 : 3·0
1	22	$+h\nu - 165$	$+h\nu - 196$	31	1 : 2·8
2	13	$+2h\nu - 112$	$+2h\nu - 137$	25	1 : 2·6
3	3	$+3h\nu - 50$	$+3h\nu - 64$	14	1 : 2·4
4	3	$+4h\nu - 29$	$+4h\nu - 42$	13	1 : 2·0
Concentrated system	71	-476	-589	123	1 : 3·0

* Omitting throughout the constant $\Delta w^1 + D^1$.

Without this term the splitting is comparable to the Davydov splitting of a concentrated system, with the exception of additional interaction terms in our case between different vibronic (electronic × vibrational) levels of the same electronic state.

FIG. 1. $A_g - B_{2u}$.

FIG. 2. $A_g - B_{1u}$.



Crystal spectra of a transition with the intensity and vibrational structure of the anthracene 3800 Å *system, assumed to belong to the long axis-polarized species* $A_g - B_{2u}$ (Fig. 1) *or the short-axis polarized species* $A_g - B_{1u}$ (Fig. 2).

Dotted lines: oriented gas model. Faint full lines: weak-coupling model with first-order energy corrections only. Full lines: weak-coupling model including intensity transfers and second-order energy corrections. The vertical lines are proportional to intensities with the *a* component above and the *b* below the horizontal line. The vertical scale is doubled in Fig. 2. The horizontal axis is marked in thousands of wave numbers. The neglected integrals D would if included, displace the crystal spectra bodily to lower frequencies.

The progression intervals in vapour and solution are constant except for a very slow change due to anharmonicity which is in any case negligible in the first few members. Crystal forces distort the intervals enough to be detectable experimentally, and do so to different degrees in the two assumed polarizations. The calculated splittings are equally characteristic, as also are the striking changes in polarization ratio; the values in the Tables should be compared with oriented-gas values of 16 : 1 and 1 : 7·8, respectively. These three quantities, the resonance splittings, the progression intervals, and the polarization ratios, are the essentially crystalline spectral properties, and they should enable the assignment of molecular transitions in anthracene and in other cases of favourable crystal structure.

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The Polarized Spectrum of Anthracene. Part III. The System at* 3800 Å.

By D. P. Craig and P. C. Hobbins.

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As briefly noted earlier (*Nature*, 1953, **171**, 566) the long-wavelength absorption system of anthracene (3750 Å in the vapour spectrum) has been studied in thin crystals at room temperature, at −140° and at about −250°, in polarized light. Frequencies and wavelengths of the absorption maxima are reported in each polarization, having been measured in several crystals at each temperature. Optical densities in the two polarizations, integrated optical densities, and the derived quantities *density ratio* and *polarization ratio* are reported to a precision limited by loss of light owing to reflection at the crystal surfaces and by the difficulty of measuring the high optical densities of the absorption maxima. Analysis of the results and comparison with the theory given in Part II * require the assignment of the absorption system to the short-axis polarized transition $A_g - B_{3u}$.

The quantities which characterize the vapour absorption spectrum of a polyatomic molecule are the wavelengths or frequencies of the bands and the intensities of the transitions recorded in them. In only the very simplest polyatomic compounds is the rotational structure of the bands resolvable with ordinary prism spectrographs and even the bands themselves rapidly become so numerous that they merge together into broad unresolved groups. In solution these band groups, each consisting of very many bands clustered about a central frequency, are the major features of the spectrum. Usually in aromatic molecules there is one prominent progression, corresponding to the excitation of successive quanta of a single vibrational motion. In benzene the progression spacing is 920 cm.$^{-1}$, which is the frequency of the " breathing " vibration in the electronically excited state; in anthracene the spacing is about 1400 cm.$^{-1}$, presumably the frequency of one of the totally symmetrical vibrations. The vibrational structure is even more blurred in crystal spectra at room temperature, but becomes better resolved when the crystal is cooled.

In polarized light new features appear in the spectrum of the crystal characteristic of the regular arrangement of identical molecules close to one another. Naturally these new features are related to the properties of the isolated molecules and, once this relationship is theoretically understood, crystal spectra can help in assigning the molecular transitions to their symmetry species. In Part I (*loc. cit.*) the very strong absorption at 2500 Å (40,000 cm.$^{-1}$) was assigned to $A_g - B_{3u}$ from its characteristic transformation in the crystal, and in this Part we similarly analyze the weaker 3800-Å system. The cases are different in some important respects, notably that in the strong system the size of the Davydov splitting and qualitative intensity relations decide the issue, whereas here we must use subtler changes in frequency between the polarizations and rely more on measured optical densities and intensities, the significance of which has been detailed in Part II (*loc. cit.*).

The Polarization Ratio.—The two quantities characteristic of the crystal spectrum which are most valuable for interpreting the measurements to be reported in this paper are the *Davydov splitting* treated in Part I and a new quantity, the *polarization ratio*, now defined. Given the optical densities $E_a(\nu)$ and $E_b(\nu)$ for light polarized parallel to the *a* and *b* crystal axes we obtain directly the *density ratio* E_a/E_b, evaluated from the maximum values in the two polarizations. The theoretical significance of this quantity is not simple for reasons given later, and we prefer wherever possible to evaluate the ratio of the integrated optical densities over corresponding * bands or groups of bands:

$$P = \int E_a(\nu)\mathrm{d}\nu / \int E_b(\nu)\mathrm{d}\nu$$

The polarization ratio is the more fundamental quantity because $\int E_a(\nu)\mathrm{d}\nu$ and $\int E_b(\nu)\mathrm{d}\nu$ are

* Parts I and II, *J.*, 1955, 539, and preceding paper.

each proportional to the oscillator strengths of transitions in the crystal and so may be connected with the free-molecule oscillator strengths by the theory of Part II. Well-known relations between transition moment and oscillator strength being used [Part II, equation (13)], the polarization ratio is

$$\left\{\mathscr{M}^{\alpha} \cdot \mathbf{a}/|\mathscr{M}^{\beta}|\right\}^2(\nu^{\alpha}/\nu^{\beta})$$

where $\mathscr{M}^{\alpha}$ and ν^{α} are the transition moment and frequency of maximum absorption in the a component. In the practical case $\nu^{\alpha} \cong \nu^{\beta}$, and the polarization ratio is nearly enough equal to the squared ratio of transition moments. The density ratio on the other hand is useful in this fundamental way only if it is equal to the polarization ratio, *i.e.*, only if the band groups in the two polarizations have geometrically similar shapes, and this requires a similarity in the intensity distribution amongst vibrational sublevels which is not necessarily realized. In practice the density ratio shows variations from crystal to crystal and from band group to band group which, aside from all questions of theoretical significance, make it somewhat unsatisfactory as a characteristic property of the system.

Measurements at 20° and 60°.—Our results divide into sets according to the temperatures at which the spectra were recorded, *viz.*, 20°, 60°, −140° and the temperature of boiling hydrogen (−250°). At −250° the number of measurements was restricted by supplies of liquid hydrogen, but at the higher temperatures the spectra of some ten crystals were measured and the results averaged. Fig. 1 illustrates a typical set of results for a crystal about 0·2 μ thick at 20°. The spectrum at room temperature is poorly resolved. In each polarization there are three maxima separated to a first approximation by 1400 cm.$^{-1}$ as in solution; their relation to the vapour and solution peaks is at once apparent, with a displacement to lower frequencies by about 2000 cm.$^{-1}$ from the vapour. They will be described as forming the A progression with members A_a^0, A_a^1, A_a^2 in a polarization and A_b^0, A_b^1, and A_b^2 in b polarization. Table 1 lists wave-

TABLE 1. *Wavelengths and frequencies at 20° and 60°.*

	20°		60°	
	Wavelength (A)	Frequency (cm.$^{-1}$)	Wavelength (A)	Frequency (cm.$^{-1}$)
A_a^0	3922 ± 1	25,497	3920·5 ± 1	25,507
A_b^0	3931 ± 10	25,439	3933 ± 9	25,426
A_a^1	3716 ± 1·4	26,911	3714 ± 1	26,925
A_b^1	3725 ± 4	26,846	3722 ± 1·5	26,867
A_a^2	3524 ± 0·7	28,377	—	—
A_b^2	3529 ± 1·7	28,337	3523 ± 1·5	28,385

* The idea of corresponding bands has force only in terms of the weak-coupling model treated in Parts I and II, where one thinks of a band in a polarization and another in b as a pair derived by perturbing one free-molecule band.

lengths and frequencies for these maxima at 20° and 60°. The errors are standard deviations, based usually on five or six measurements at 20° and four at 60°. Measurements of the b maxima show considerable scatter and are not precise enough except in one or two cases in Table 1 for calculating the Davydov splitting and other frequency differences. There is a barely significant temperature displacement of wavelengths between 60° and 20°; we believe it to be real, since a further displacement in the same sense occurs between 20° and −140°. The difference between the frequency of the n-th maximum in one polarization and the corresponding maximum in the other is measured by $A_a^n - A_b^n$: we continue to describe this interval as the Davydov splitting, although as shown in Part II it arises only partly from the effect which Davydov considered and partly from second-order effects. We are concerned also with the intervals to be referred to as *progression intervals* between successive maxima in a given polarization, measured by differences of the type $A_a^1 - A_a^0$. These intervals in vapour and solution are constant, but are disturbed rather irregularly in the crystal. Values of some derived quantities are listed in Table 2, based on the more precise results in Table 1.

The increased progression interval between the second and third members is significant

and is confirmed by measurements at lower temperatures. Its importance is discussed below.

The optical densities of the crystals in the two polarizations were measured as described in Part I and the density ratios found. These ratios are unsuitable for averaging because

TABLE 2. *Splittings and progression intervals at room temperature.*

Davydov splitting		Progression intervals (solution value 1412 cm.$^{-1}$)			
$A_a^1 - A_b^1$	65 ± 31 cm.$^{-1}$	$A_a^1 - A_a^0$	1414 ± 12 cm.$^{-1}$	$A_b^2 - A_b^1$	1491 ± 32 cm.$^{-1}$
$A_a^1 - A_b^1$	58 ± 13	$A_a^1 - A_a^0$	1418 ± 10	$A_b^2 - A_b^1$	1518 ± 16
$A_a^2 - A_b^2$	40 ± 5	$A_a^2 - A_a^1$	1466 ± 12		

of the varying reflection loss from the crystal surfaces. This may be equivalent to an optical density in the range 0—0·10 or even 0·15 added to the desired optical density due to absorption. The crystals used are less than a wavelength thick and interference effects

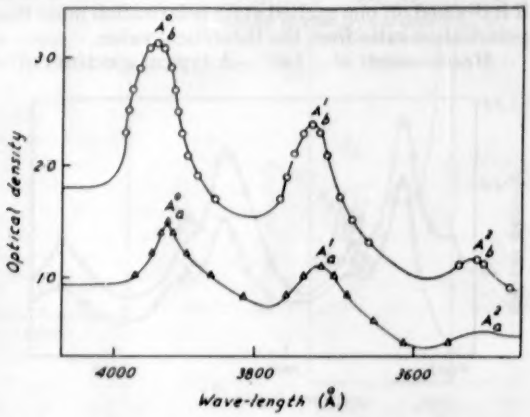


FIG. 1. *Polarized spectrum of anthracene at 20°.*
Upper curve: absorption parallel to *b* crystal axis.
Lower curve: absorption parallel to *a* crystal axis.

complicate the reflection behaviour *; under these conditions the dependence of loss on crystal thickness and on wavelength is bound to be sensitive. Reflection is relatively less important compared to molecular absorption for thick crystals than for thin; but thick crystals have high optical densities intrinsically more difficult to measure accurately. The results for several crystals are set out in Table 3. No correction to these values has been made for the reflection loss.

These values are very scattered. A nearly constant set of results is found by measuring the polarization ratio, recorded in Table 4 for three different crystals for which results were available complete enough to carry out the required integrations of optical density.

TABLE 3. *Density ratios (E_a/E_b) at absorption maxima (20° and 60°).*

A^0	A^1	A^2	A^0	A^1	A^2
—	—	1/1·8	1/1·9 *	1/1·8	1/1·5
1/2·4	—	—	1/1·9 *	1/1·7	—
—	—	1/1·7	1/1·7 *	1/1·8	1/1·8
1/2·1	1/2·7	—	1/2·3 *	1/1·8	1/1·4
1/1·6	1/1·7	1/1·4			

* At 60°.

TABLE 4. *Polarization ratios at 60°.*

A^0	A^1	A^2	Overall
1/2·0	1/1·7	1/1·4	1/1·7
1/2·0	1/1·8	1/1·7	1/1·8
1/2·1	1/1·6	1/1·4	1/1·7

Values of the polarization ratio have not previously been recorded, and the only result which is at all comparable relates to a measurement of the fluorescence emission of crystalline anthracene by Ganguly and Choudhuri (*J. Chem. Phys.*, 1951, **19**, 617). There

* Dr. L. E. Lyons kindly drew our attention to cases in which the transmission of a silica disc plus thin crystal is greater than that of the disc alone, suggesting a negative reflection loss by the principle of the coated lens.

is a well-known mirror symmetry between absorption and fluorescence in vapour and solution spectra and reference to the theory of Part II shows that this principle has an application also in crystals. Fluorescence is predominantly from the lowest excited state and one should find that the emitted light is polarized in the same ratio as the light absorbed in the first member of the absorption progression. The overall polarization ratio in fluorescence should therefore be near to, but slightly greater than, the overall ratio in absorption. Ganguly and Choudhuri analyzed the fluorescence emission with an optical system with which they could find the direction of maximum intensity in relation to the crystal axes. They found that this direction made an angle of 33° with the *b* crystal axis, a result which may be interpreted to mean that the *b* polarized emission is $\cot^2 33° = 2{\cdot}4$ times stronger than the *a* emission. This is greater than the overall absorption ratio (1·8) and even somewhat greater than the ratio for A^0 (2·0). The agreement must however be treated with caution, since a fraction of the excited molecules lose their energy otherwise than by fluorescence. Little is known of the details of this degradation which, if it drained off one excited state polarization more than the other, could upset the emission polarization ratio from the theoretical value.

Measurements at −140°.—A typical spectrum at −140° is illustrated in Fig. 2. Com-

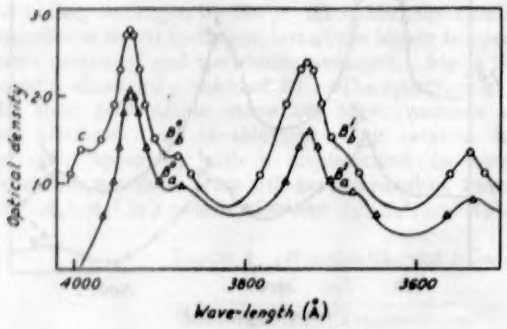


FIG. 2. *Polarized spectrum at* −140°.
Upper curve : parallel to *b* crystal axis.
Lower curve : parallel to *a* axis.
The three main maxima are the *A* series, as in Fig. 1.

pared with room-temperature spectra its maxima are better resolved and additional structure has appeared. B^0 and B^1 appear in both polarizations and clearly form the beginning of a progression distinct from the *A* series; band *C* shows only in *b* absorption, and no corresponding *a* absorption was found in any of the crystals examined at this temperature. Table 5 lists the wavelengths averaged over results for eight crystals.

TABLE 5. *Wavelengths and derived quantities at* −140°.

Wave-length (Å)		Frequency (cm.$^{-1}$)	Derived quantities	
A_a^0	3931·5 ± 1·3	25,436	Davydov splitting (cm.$^{-1}$)	
A_b^0	3934 ± 1	25,419	$A_a^0 - A_b^0$	17 ± 11
B_a^0	3874·5 ± 1	25,810	$A_a^1 - A_b^1$	29 ± 10
B_b^0	3880 ± 1	25,773	$A_a^2 - A_b^2$	48 ± 15
A_a^1	3725 ± 1·2	26,846		
A_b^1	3729 ± 0·7	26,817	Progression intervals (cm.$^{-1}$)	
B_a^1	3674 ± 0·7	27,218	$A_a^1 - A_a^0$	1410 ± 12
A_a^2	3532 ± 1	28,313	$A_b^1 - A_b^0$	1398 ± 9
A_b^2	3538 ± 1·5	28,265	$A_a^2 - A_a^1$	1467 ± 12
C_b	3989·5 ± 1·7	25,066	$A_b^2 - A_b^1$	1448 ± 13
			$B_a^1 - B_a^0$	1408 ± 9

The optical densities of all eight crystals were measured and values of the density ratio derived. Averaged values for the three members of the *A* progression, reflection losses being disregarded, are : A^0 1/1·4, A^1 1/1·6, A^2 1/1·7, and B^0 1/1·7. The density ratios show a very considerable scatter, but as at room temperature (Table 4) the overall polarization ratios are markedly constant in the range 1·7—1·8. Moreover in one crystal studied both at room temperature and at −140° the polarization ratio showed no change with temperature.

Measurements at about 20° K.—A limited number of spectra were recorded at the temperature of boiling liquid hydrogen in a specially constructed cell described below. The most complete single set of results is shown in Fig. 3. Structure at the long wavelength onset of absorption was partly obscured by heavy plate blackening in the spectrum illustrated in Fig. 3; in a thicker crystal more structure was visible. This is shown in Fig. 4, and the new bands are recorded in Table 6. Two crystals only could be studied at this temperature and the accuracy of the measurements is difficult to assess. Where a standard deviation is shown several measurements have been made and averaged, otherwise only one or two. The maxima were, however, in general much sharper than at −140° and an individual measurement correspondingly easier to make precisely.

The shift to longer wavelengths with decreasing temperature is confirmed by these values. The Davydov splittings and progression intervals derived from Table 6 agree within

FIG. 3. *Polarized spectrum at about* −250°.

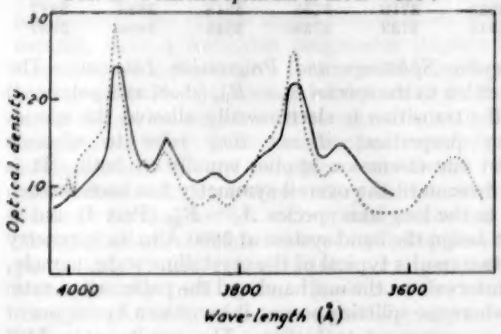
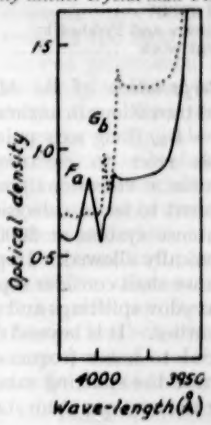


FIG. 4. *Long-wavelength onset of absorption at about* −250° *obtained with a slightly thicker crystal than* FIG. 3.



reasonable limits with values obtained at −140°. The main importance of these measurements however, to be discussed on p. 2315, is in showing variations of the density ratio in different regions of the spectrum. In the ranges where absorption is weak, absorption in *a* polarization is greater than in *b*, but where absorption is strong the *b* component is

TABLE 6. *Measurements at* −250°.

	Wavelength (Å)	Frequency (cm.$^{-1}$)		Wavelength (Å)	Frequency (cm.$^{-1}$)
F_a	4002	24,988	D_a^0	3828	26,123
G_b	3995 ± 1	25,031	D_b^0	3830	26,110
C_a	3991	25,056	A_a^1	3733 *	26,788
C_b	3989 ± 1·5	25,069	A_b^1	3738 *	26,752
A_a^0	3945 *	25,349	B_a^1	3680 *	27,174
A_b^0	3945 ± 2	25,349	B_b^1	3686 ± 0·8	27,130
B_a^0	3884 ± 0·8	25,747	A_b^2	3546	28,201
B_b^0	3887 ± 1	25,727			

* Single measurement only.

stronger than *a* (Fig. 3). At higher temperatures *b* absorption exceeds *a* throughout the system.

We are able to compare our results at this temperature with those of Obreimov and Prikhotjko (*Phys. Z. Sowjetunion*, **1936**, **9**, 34) who were the first to record a low-temperature crystal spectrum in polarized light. Their work established the general character of the crystal spectrum and showed *b* absorption to be greater than *a*. For reasons connected with the low dispersion of the spectrograph, their wavelength measurements were not exact enough to prove a Davydov shift nor to establish perturbations in the vibrational

intervals, and there are some minor features of their results, such as a splitting in the intense *a* maximum, which our plates do not show. More important is their conclusion that there are several very sharp bands in the *b* spectrum which are missing in the *a*, namely at 4037, 4005, 3991, 3981, 3916, 3857, 3848, and 3805 Å. The strongest of these is at 3991 Å, band *C* in Table 6. There is no doubt that this occurs in both polarizations as shown in Fig. 4; its *a* component however was only detected at low temperatures and in a rather thick crystal, otherwise it tends to be hidden by A_a^0. Not all of the other bands were visible under the conditions used for our plates, but those which do appear, such as F_a at 4002 Å, seem to do so always in both polarizations even though as in this case the weaker component is ill-defined. Clearly, more work at very low temperatures will be needed to study these sharp and weak bands, but our work goes to show that they have components in both polarizations and do not therefore call for a novel explanation. Table 7 compares some wavelength values from Obreimov and Prikhotjko (*loc. cit.*) with ours.

TABLE 7. *Wavelengths* (Å).

Band group	A_a^0	A_b^0	A_a^1	A_b^1	A_b^2	B_a^0	B_b^0
Obreimov and Prikhotjko ...	3940	3938	3719	3735	3548	3885	3887
Present work	3945	3945	3733	3738	3546	3884	3887

Interpretation of the Measured Davydov Splittings and Progression Intervals.—The allowed transitions in anthracene belong either to the species $A_g - B_{2u}$ (short axis polarized) or $A_g - B_{3u}$ (long axis polarized). If the transition is electronically allowed the species symbols refer to electronic symmetry properties; if not they refer to vibronic (electronic × vibrational) symmetry and our discussion applies equally to both. It is convenient to leave a decision between them until the overall symmetry has been settled. The intense system at 2500 Å belongs to the long axis species $A_g - B_{3u}$ (Part I) and is electronically allowed. In proceeding to assign the band system at 3800 Å to its symmetry species we shall consider separately the two results typical of the crystalline state, namely, the Davydov splittings and progression intervals on the one hand and the polarization ratio on the other. It is beyond doubt that, where the splitting occurs, it involves a *b* component displaced to lower frequencies and an *a* component to higher. The results at −140° determine the splitting most accurately (Table 5). It is in the range 10—50 cm.$^{-1}$, and is less for the zero-quantum state than for the others. Table 8 compares the values at −140°

TABLE 8. *Calculated and found values of splittings and progression intervals at* −140°.

	Davydov splitting (cm.$^{-1}$)			Progression intervals (cm.$^{-1}$)			
	Found	Calc. for $A_g - B_{3u}$	Calc. for $A_g - B_{2u}$		Found	Calc.* $A_g - B_{3u}$	Calc.* $A_g - B_{2u}$
A^0	17	217	29	$A_a^1 - A_a^0$	1410	1483	1427
A^1	29	282	31	$A_b^1 - A_b^0$	1398	1418	1425
A^2	48	225	25	$A_a^2 - A_a^1$	1467	1397	1465

* By taking the vapour splitting as 1412 cm.$^{-1}$.

with values calculated in Table 2 of Part II for the two allowed assignments in anthracene. The splittings are incompatible by an order of magnitude with the long axis assignment $A_g - B_{3u}$ but they agree as well as can be expected with the short axis $A_g - B_{2u}$. The progression intervals, also in Table 8, give a less definite indication; the best established experimental fact is that the interval $A^2 - A^1$ is greater than $A^1 - A^0$ by a substantial margin outside the experimental error. This feature appears in calculations for $A_g - B_{2u}$ and not for $A_g - B_{3u}$ and so the former assignment is supported; the numerical agreement is not, however, uniformly good.

Interpretation of the Measured Polarization Ratio.—The theoretical value of the polarization ratio in a weak system has been discussed in Part II (*loc. cit.*). For the oriented gas model a long and a short axis system are associated respectively with ratios 16 : 1 and 1 : 7·8. According to Part II a weak system would not give values at all close to these. For a system like that of anthracene at 3800 Å, due allowance being made for a strong long axis system nearby, the calculated values are near 2·3 : 1 and 1 : 3·0. These figures apply to a weak system which in the free molecule is entirely of one polarization. However, aside

from crystal perturbing forces it is possible that intramolecular vibrations may also transfer intensity from strong transitions to weaker ones. The only well-understood example of vibrational perturbations in a complex molecule is that of benzene where the whole of the intensity in the 2600 Å system ($f = 0{\cdot}002$) and in the 2000 Å system ($f = 0{\cdot}1$) is vibrationally induced. Herzberg and Teller's theory of the effect (*Z. phys. Chem.*, **1933**, **21**, *B*, 410) shows the borrowed intensity to be proportional to the first power of the intensity of the perturbed strong system and to the inverse square of its energy separation from the weak one. Assuming other factors to be equal, and noting that the intense system in anthracene is twice as strong as in benzene, we find that the stolen intensity in the 3800 Å anthracene system is between $f = 0{\cdot}005$ and $0{\cdot}05$. Its polarization, like that of the strong system, must be parallel to the long axis, and from the crystal structure the stolen intensity amounts to between $f = 0{\cdot}0037$ and $0{\cdot}037$ along the *a* axis and one sixteenth as much along *b*. These are probably minimum values because in bigger molecules the vibrational amplitudes are usually greater, so that one expects an increased effect in anthracene; but a value within these limits will account for the observed results. Vibrationally borrowed intensity would not coincide with the maximum of the allowed component; the system might behave as do substituted benzenes in the 2600 Å system, namely, have a forbidden progression displaced from the allowed progression by the frequency of a non-totally symmetrical vibration, and, provided the forbidden intensity were great enough, it should be detectable in the troughs between the allowed maxima, especially as its polarization is opposite, with $E_a > E_b$. In spectra at liquid-hydrogen temperature (see p. 2313) such regions were found which suggested that the system was a mixture of allowed and forbidden components. The resolution of the *a* polarized zones is poor and since they are of secondary importance to the assignment of the main system they were not studied further. Compared to the wavelength measurements, which are fairly straightforward, measurements of crystal optical densities are subject to at least two errors, particularly when considerations of crystal thickness demand the measurement of inconveniently high optical densities. The errors introduced by reflection have been discussed (p. 2311). We have no satisfactory measure of the reflection loss but, by analogy with the properties of light in transparent media, take it to correspond, at most, to an effective optical density of 0·1—0·15 unit. The contribution of reflection to the measured intensites $\int E_a d\nu$ and $\int E_b d\nu$ may be assessed and subtracted; the range of integration is about 3600 cm.$^{-1}$ and the reflection "intensity" is therefore about 360, or 540 in the extreme case. In a typical measurement the measured ratio is 8500/4700 = 1·8; the maximally corrected value falls near 1·9. Evidently the correction is small even under extreme conditions.

The second error arises when, in measuring high values of the optical density, we compare the plate blackening by light which has passed through the crystal with that in which a high optical density has been simulated by a rotating sector and a reduced time of exposure. Failure of the photographic reciprocity law may then give incorrect results (see p. 2318 for a detailed discussion). Essentially, high values tend to be measured as too high, making the density ratio and, to a lesser extent, the polarization ratio, high also. This effect was minimized by using the reduced exposure method only where absolutely necessary, *i.e.*, in the highest optical densities. Thus the wavelength range over which the error can occur, and the error in the integrated optical density, are small; it could not exceed 0·1 in the polarization ratio, reducing the measured 1·8 to 1·7. On the other hand the density ratio is very sensitive to the values at the maxima and this probably explains its erratic behaviour.

We now consider actual values. The calculated values in Table 2 of Part II show that the system must be assigned to $A_g - B_{2u}$ and not $A_g - B_{3u}$. The latter requires a polarization behaviour in which the *a* component is the stronger, which conflicts with experiment, whereas the former makes the *b* component stronger, as is actually found. The experimental ratios, with those calculated given in parentheses, are 1/2 (1/3), 1/1·7 (1/2·8), 1/1·5 (1/2·6). The discrepancy arises mainly from the mixture with the main system of a vibrationally induced long axis component and not from the small reflection and reciprocity

errors, which oppose one another. We consider that the vibrationally induced intensity is about 20% of the whole. This leads to a reasonably satisfactory agreement, but neither the theoretical nor the experimental accuracy justifies elaborate computations. We now consider whether the system $A_g - B_{2u}$ is electronically allowed or, like the long axis component, allowed only through vibrational perturbation of some other system. There is no direct evidence from our measurements but two arguments are against assignment to an electronically forbidden transition. First, it is improbable on grounds of magnitude. The nearest intense short axis system begins near 2000 Å, separated by 25,000 cm.$^{-1}$ from the weak system. By analogy with benzene, intensity borrowing here would not exceed $f = 0{\cdot}02$, only one fifth of the observed value. Secondly, experience suggests that a forbidden system would reveal itself in solution, as in benzene, with a weak but definite 0—0 band to long wavelengths of the main system. The careful study of the solution spectrum over a range of temperature and down to very low values of extinction coefficient made by Broderson and Langseth (*Dansk Mat. Fys. Medd.*, 1951, **3**, 26) would have shown such structure if it existed, but none was found. The assignment is therefore to the allowed *electronic* species $A_g - B_{2u}$.

A further confirmation is in the comparison of the total intensity of the weak system in the crystal with that in solution. The necessary geometrical relations between solution and crystal values were given in Part I. A short axis system, before allowance for interaction with other systems, should have an optical density per micron of $2{\cdot}17 \times 10^{-4}E$, parallel to the *a* axis and $1{\cdot}69 \times 10^{-3}E$, parallel to *b*, E, being the solution extinction coefficient of about 10^4 units. The transfer effect makes little difference to the *b* component, which is better for this comparison. Our crystals were 0·1—0·2 micron thick, and the *b* optical density should have fallen in the range 1·7—3·4: its value was usually near 3·0, in good agreement with expectation and in further support of the short axis assignment.

Short axis polarization has been widely credited to this system in anthracene, mainly because of the molecular-orbital prediction discussed below. Most previous experimental work has been done with unpolarized light and so is not relevant. Obreimov and Prikhotjko (*loc. cit.*) and Ganguly and Choudhuri (*loc. cit.*) showed respectively that absorption and fluorescence are stronger along the *b* than the *a* axis, but these results could not be interpreted until the assignment of the intense system at 2500 Å was established. Aside from our earlier report (*Nature*, 1953, **171**, 566) the only relevant work is the spectrum of anthracene in durene (McClure, *J. Chem. Phys.*, 1954, **22**, 1256). Making reasonable assumptions about the orientation of the embedded molecules McClure found absorption to be concentrated along the short axis and assigned the system $A_g - B_{2u}$, in agreement with us. Jones (*Chem. Rev.*, 1947, **41**, 353), without using polarized light, but by studying the spectral effects of substitution in different positions in anthracene, came to the same conclusion.

Comparison with Theory.—Energy levels of anthracene have been calculated by at least three distinct forms of π-electron theory. Forster (*Z. phys. Chem.*, 1938, **41**, *B*, 287) used the valence-bond method and predicted that the lowest singlet excited state would be of species B_{3u}, a conclusion which we have shown to be incorrect. Coulson (*Proc. Phys. Soc.*, 1948, **60**, 157) and Platt (*J. Chem. Phys.*, 1950, **18**, 1168), using molecular-orbital theory in its LCAO and free-electron forms, respectively, predicted correctly that the first excited state would be B_{2u} and the second B_{3u}. Moffitt (*J. Chem. Phys.*, 1954, **22**, 320) has recently developed Platt's scheme and made possible quantitative calculations of transition energies and oscillator strengths. Having now two experimentally established assignments in anthracene, we may compare the true oscillator strengths with values calculated in the LCAO–MO theory and in Moffitt's *perimeter model* (Table 9).

TABLE 9. *Calculated and found oscillator strengths in anthracene.*

	Experimental	LCAO-MO	Perimeter model
Lowest singlet	$A_g - B_{2u}$: f . . . 0·1	0·9	0·37
Second singlet	$A_g - B_{3u}$: f . . . 2·3	1·4	4·8

LCAO–MO theory appears to be equally suitable for the higher linear polycyclic hydrocarbons tetracene and pentacene, but not for naphthalene. According to theory, naphthalene should show the same sequence of ultraviolet-band systems as anthracene,

with somewhat higher transition energies; but the spectrum shows an additional very weak band system at 3200 Å which cannot be fitted into the LCAO–MO scheme. This weak system is found in free-electron calculations, in those based on the perimeter model, and in the non-empirical configurational interaction approximation (Jacobs, *Proc. Phys. Soc.*, 1949, **62**, 710): the predicted assignment is $A_g - B_{3u}$. This is one of two assignments which are compatible with experimental evidence, the earlier part of which has been reviewed by one of us (Craig, *Rev. Pure Appl. Chem.*, 1954, **3**, 207).

Experimental

The Crystals.—Anthracene (B.D.H. " blue fluorescing ") was purified by chromatography on alumina in light petroleum (b. p. 40—60°) in darkness to avoid photo-oxidation of adsorbed anthracene to anthraquinone, which occurs rapidly in daylight. The pure anthracene was eluted and crystallized (m. p. 218°). It did not phosphoresce with ultraviolet light when dissolved in a rigid glass of ether–2-methylbutane–alcohol.

Thin crystals were produced by rapid sublimation in an inert atmosphere. A small cylindrical furnace made from 1" copper tube 1·5" long and wound with a 50-ohm heating coil encased in fireclay was placed on a hot-plate. A Pyrex beaker fitted the furnace; the hot-plate was heated initially to 100° and the beaker filled with solid carbon dioxide or with nitrogen gas. A small amount of anthracene was put in and the heater closed by a filter paper held down by a crucible lid. The hot-plate was then switched off and the heater run at 1·5 A for 1—2 min. Sublimation continued for 5—10 min.; crystals formed inside the porcelain lid and on the filter paper. The former were usually thinner, varying with the conditions; the thinnest showed blue or golden interference colours and were 0·1—0·2 μ thick. Measurements were usually made with the crystals mounted on a polished silica disc to which they were transferred on an electrically charged needle from the sublimation surface.

Obreimov and Prikhotjko (*loc. cit.*) reported that sublimation leaflets of anthracene crystallize regularly and in the (001) orientation. This was of central importance to our work, and at our request Dr. Philip Knight of the Department of Crystallography, University College, made a number of *X*-ray examinations of crystals of different thicknesses and from different batches to confirm it. The orientation was always found to be (001). The well-developed crystal face thus contains the *a* and *b* monoclinic axes, and it was found by microscopy that the *b* axis corresponded to the slow vibration direction. This fact allowed all other crystals to be aligned with their *a* and *b* axes along the electric vector vibration directions by microscopy alone.

We had no very satisfactory way of measuring crystal thickness but used the two following approximate methods. (i) From Newton's colour scale retardations were found by identifying interference colours. The thickness d is then given by the formula $R = d(\beta - \alpha)$, where the bracketed quantity is the birefringence in the ab plane, R is the thickness, and d the retardation. For anthracene, $R = d(1{\cdot}79 - 1{\cdot}63)$. (ii) The surface area of a thin crystal was estimated as closely as possible. The crystal was dissolved in a known volume of alcohol and the optical density of the solution measured with a Cary recording spectrophotometer in the region of intense absorption near 2500 Å. The concentration of the solution being thus determined, the thickness of the crystal was calculable. The agreement with (i) was within a factor of 2 and is the basis for the earlier statements here and in Part I that the thickness of the best crystals was about 0·1—0·2 μ.

Spectroscopic Methods.—Two spectrographs, Hilger types E1 and E492, both large quartz Littrow instruments with the same optics, were used. The plates used were: 4500—3000 Å, Ilford Special Rapid; 3000—2500 Å, Ilford Q1; 2500—2000 Å, Ilford Q2.

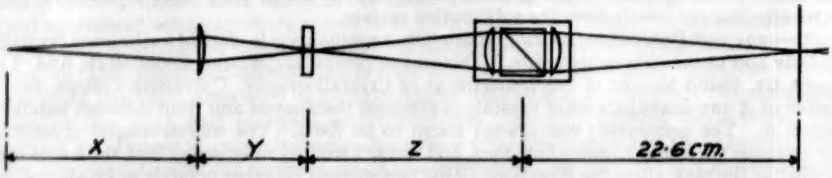
For work below 3500 Å a small 500 mA hot cathode hydrogen discharge lamp was used as the light source, running at constant voltage. Above 3500 Å the stray line spectra from the hydrogen lamp were disturbing and the best source was a Siemens P28/25 strip lamp running at 6 V, 18 A. The lamp was mounted with the tungsten strip in a horizontal plane to minimize temperature variations. Light from the strip was reflected into the optical system from an aluminium mirror at 45°. In experiments with a rotating sector it was necessary to run the lamp from accumulators to eliminate beat effects between the periods of the sector and brightness fluctuations.

Light from the source was focused on to the crystal in its holder by a fused silica lens (Fig. 5). The transmitted light entered the Wollaston unit and came to a pair of foci at the slit, each plane polarized, and with the planes perpendicular to one another. The separation of the beams was

4 mm. The Wollaston unit held the prism itself (2 cm. aperture) and two plano-convex fused silica lenses of focal length 20 cm. at 3200 Å facing opposite sides of the prism and adjustable so that parallel light entered the prism at any chosen wavelength. Careful alignment was necessary to ensure that both beams in a blank exposure have the same intensity. This condition was satisfied when both beams illuminated the same area of the spectrograph prism symmetrically about its centre line.

Microphotometer records were taken of all plates by use of a Zeiss microphotometer. Iron-arc spectra were photographed on the plate between the two polarized crystal absorptions and each microphotometer record was run twice, once to draw the trace of the absorption and a second time to draw the iron arc spectrum. The record was then read with a travelling microscope, wavelengths being measured by linear interpolation between closely spaced iron lines. The method for measuring optical densities has been briefly described in Part I. A series of blank exposures was made with the same exposure time as for the absorption spectrum of the crystal. Successive exposures were reduced in intensity by a rotating sector, giving a set of plate blackenings corresponding to known optical densities. The spectrum of the crystal was then recorded on the microphotometer on the same record as an optical density blank. The traces crossed at "match points." From a set of such records values of optical density were assembled as a function of wavelength. The error introduced by a second more convenient method was found to be negligible: this was to superimpose a trace of the absorption spectrum upon traces of known, sectored, optical density taken from a second plate developed under identical conditions, and then to measure the wavelengths of the match points.

FIG. 5. *External optical system showing the source at the left-hand end, then a fused silica lens, the crystal holder, the Wollaston prism unit, and the spectrograph slit at the right. $X + Y + Z = 24{\cdot}2$ cm. The Wollaston unit as a whole was kept fixed, but the two lenses in it were movable, to allow the light through the prism to be made parallel at any wavelength.*



Our programme of measuring optical densities of the same crystal in two polarizations made it inevitable to work at higher optical densities than available with a rotating sector. The two polarizations differ in intensity by a factor of about 2, so that even if one can be measured at the optimum density, say 0·8, the other is unfavourably high or low. The method used for high optical densities involved as an extra feature a fixed sector setting and logarithmically decreasing exposure times, beginning with the same exposure as used for the crystal spectrum (15 min.). An undesirable aspect is the possible failure of the photographic reciprocity law but by using the variable exposure method only for the highest optical densities, and by repeating all measurements of density and polarization ratio on several crystals of different thickness we could ensure that the errors were small. The optical densities measured by varying the exposure tend to be high: the photographic efficiency for short exposures of the emulsions used is greater than for the 15 min. crystal exposures, giving greater plate blackenings in the comparison runs than for strict proportionality. Match points are obtained with spuriously short comparison exposures, and therefore at too high optical densities. Published curves suggest a maximum error of 0·3 density units under our conditions. This error, if it occurred, would be directly shown in the density ratios which tend to be too high; but its effect is rather small in the polarization ratio, since the integrated intensities are affected only by a small part of the range of integration, and for the greater part the density values involve no reciprocity error at all (sector method) or a negligible one (exposure ratio 5 : 1 or less).

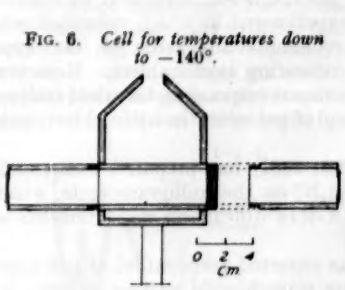
Low-temperature Cells.—A very simple cell (Fig. 6) was found adequate for temperatures in the range 60° to −140°. One face of a hollow brass cube of side 8 cm. was removed and replaced by a hollow pyramid, with a 2·5 cm. square opening at the top. Two round holes were drilled in opposite faces of the cube and a brass tube (3·5 cm. dia.) inserted. Two similar tubes, each having one end closed by a silica window, could be screwed into the end of this tube, making a closed cylinder of which the centre part was surrounded by the brass cube, and so cooled or heated by its contents. The centre section contained an annular stop against which the crystal

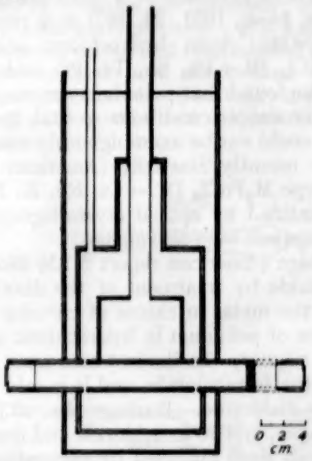
on its mount could be held. Even when liquid air was used as refrigerant no condensation took place on the crystal, but it was necessary to stop condensation on the end windows with jets of air. The temperature measured at the position of the crystal was −140° with liquid air as cooling agent.

For work with liquid hydrogen the more elaborate cell shown in Fig. 7 was constructed. In this case the central section of the tube holding the crystal joins the rest of the cell only

FIG. 7. *Cell for use with liquid hydrogen as refrigerant. Brass is used throughout except for the thin tube of German silver joining the inner reservoir and sample tube to the rest of the apparatus. The hydrogen reservoir is surrounded by an evacuated space, and the outermost container holds an alcohol–CO_2 cooling mixture.*

FIG. 6. *Cell for temperatures down to −140°.*





through the poorly conducting thin (0·1—0·2 mm.) German-silver tube to the exterior of the Dewar flask. The end pieces to which the quartz windows were fixed with Araldite cement screwed in as shown and were greased with Silicone grease as lubricant and vacuum seal. The windows were heated to keep them free from ice. At the beginning of a run the outer jacket was filled with dry ice. After 30 min. liquid oxygen was put into the reservoir and after another 30 min. the Dewar flask was slowly evacuated through a capillary, the crystal being by this time cold enough to resist damage and distortion. After another 30 min., when the last drop of oxygen had evaporated, liquid hydrogen was siphoned in and, after conditions became steady, the run was started. The crystal was probably cooled to *ca.* 20·4° K, the b. p. of hydrogen.

Several colleagues, whom we thank, helped in the work described in the three papers. Professor C. K. Ingold, F.R.S., in whose laboratories the experiments were made, assisted generously throughout; Dr. H. G. Poole designed the external optics; Dr. P. Knight made *X*-ray examinations of selected crystals; Prof. F. E. Simon, F.R.S., made gifts of liquid hydrogen and Dr. R. Berman advised us on its handling and use; and Dr. L. E. Lyons, Dr. I. G. Ross, and Mr. J. A. Ferguson criticized the manuscripts.

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The Polonium Halides. Part I. Polonium Chlorides.

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Polonium dichloride and tetrachloride have been prepared on the milligram scale and some of their chemical properties have been investigated. A chloride ammine and ammonium and cæsium hexachloropolonite have also been prepared. The dichloride is orthorhombic and ammonium hexachloropolonite is face-centred cubic. The deposition of milligram amounts of ^{210}Po on to gold foil and wire is described.

The probable existence of a quadrivalent chloride of polonium was suggested by Guillot (*J. Chim. phys.*, 1931, **28**, 107) as a result of tracer experiments in which polonium was co-precipitated from hydrochloric acid solution on ammonium salts of the type $(NH_4)_2MCl_6$ (M = Pb, Sn, Te, Pt) under conditions indicating isomorphism. However, it was also found that polonium was co-precipitated on the corresponding tervalent iridium salt under similar conditions so that the quadrivalency of polonium in hydrochloric acid solution could not be unambiguously established.

More recently Staritzky (American report LA-1286, 1951) has prepared compounds of the type M_2PoCl_6 [M = Cs, Rb, K, NH_4, and $(CH_3)_4N$] on the milligram scale, which were identified by optical crystallographic studies. *X*-Ray diffraction measurements of the cæsium salt were also made.

Burbage (American report MLM 885, 1953, 18) has reported preparation of polonium tetrachloride by treatment of the dioxide with carbon tetrachloride vapour at 200°, by heating the metal in excess of chlorine at the same temperature and by evaporation of a solution of polonium in hydrochloric acid to dryness in an atmosphere of carbon tetrachloride vapour. In the last case some dichloride was also formed by thermal decomposition of the tetrachloride, and it is said that carrying out the decomposition in a vacuum gave the dichloride. Burbage (*loc. cit.*) also describes the reduction of the tetrachloride in hydrogen, first to a dichloride and finally to what was assumed to be the metal. These compounds were analysed by estimating the polonium calorimetrically and the halogen by potentiometric titration.

Since elementary polonium is the most convenient starting material for preparations, the deposition of polonium on to gold foil and wire was investigated as a preliminary to the present work. The cathodic and anodic deposition of tracer quantities of polonium on to gold has been described by many authors (Joliot, *J. Chim. phys.*, 1930, **27**, 119; Haïssinsky, *ibid.*, 1932, **29**, 453; 1933, **30**, 27 *et seq.*). The factors influencing deposition were studied quantitatively by Joliot (*loc. cit.*), and more recently Broda and Wright (British report B.R. 641, 1945) investigated the deposition of millicurie quantities of ^{210}Po on to platinum electrodes from trichloroacetic acid solutions.

Experimental

Experimental work was carried out in dry-boxes in order to minimise the hazards associated with the high level of α-activity.

Electrodeposition on Gold.—Choice of cathode material. Wertenstein (*Compt. rend. Soc. Sci. Varsovie*, 1917, **6**, 771) and later Joliot (*loc. cit.*) noted that the deposition of polonium on to platinum does not proceed as smoothly as on to gold. Joliot attributes this to surface oxidation of the platinum under the intense α-bombardment, and Haïssinsky (*J. Chim. phys.*, 1935, **32**, 116) suggests that compound formation may take place. The observations of these authors have been confirmed and, since sublimation of polonium takes place more readily from gold than from platinum, the former was used for routine depositions.

Choice of solvent. Since polonium is very soluble in hydrochloric acid and is probably largely involved in complex-formation (*e.g.*, as $PoCl_6^{2-}$), the acid should be a suitable solvent, but the deposits obtained were patchy and tended to flake from the cathode. This may be due to the action on the electrodes of chlorine produced by the α-bombardment of the solvent, as shown by the dissolution of gold in a solution of polonium in hydrochloric acid. In the

presence of hydrazine, which acts as a depolariser and also reduces the polonium to the bivalent state, better deposits were obtained, but the method was not used owing to the difficulty of controlling the marked potential drift during the deposition. The low solubility of polonium in dilute nitric acid, and the rapid dissolution of the metal from the electrodes in concentrated nitric acid, limit the use of nitric acid as a solvent for deposition. However, a solution containing 65 mc/ml. in N-nitric acid was found satisfactory.

Electrode potential Po/Po^{4+}. The electrode potential E_0 Po/Po^{4+} has been determined on the tracer scale in nitric acid solution (10^{-13} to 10^{-8}M) by Hevesy and Paneth (*Sitzungsber. Akad. Wiss. Wien*, **1914**, **123**, 1619), Wertenstein (*loc. cit.*), Joliot (*loc. cit.*), Haïssinsky (*loc. cit.*), and Heal (Canadian Report N.R.C. 1567, 1943). The mean value of their results was $E_0 + 0{\cdot}77$ v. In the approximately 10^{-6}M-solutions employed for deposition E was found to be $+0{\cdot}68$ v, giving a value of $E_0 + 0{\cdot}76$ v. Work on the accurate determination of the electrode potential is still in progress.

Deposition apparatus. The apparatus was designed to minimise the radioactive contamination which is associated with the transfer of liquids of high specific activity. Fig. 1 shows the electrolysis cell *B*, which is connected by poly(vinyl chloride) tubing of 2-mm. internal diameter to flask *A*, which contains the stock polonium solution in nitric acid, and to flask *C*, which contains the residues from the electrolysis and is fitted with electrodes to scavenge the residual polonium. *E*, *F* are rubber bulbs fitted with one-way valves, and *G* is a simple rubber bulb.

FIG. 1.

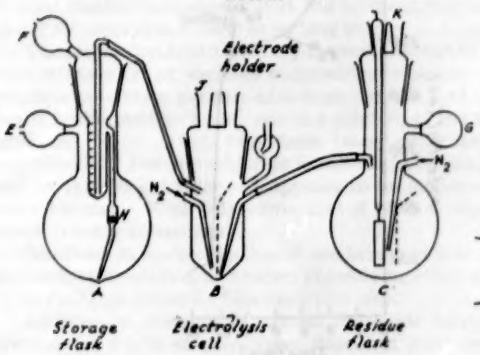


FIG. 2.

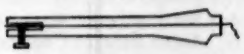


FIG. 3.

H is a one-way ground-glass valve. The required volume of stock solution is transferred into the measuring tube by manipulation of bulb *E*. On completion of the electrolysis the spent solution is sucked into the flask *C* by manipulating bulb *G*.

Joliot (*loc. cit.*) considered that the efficiency of deposition was increased by rapid stirring but, since it was undesirable to leave a stirrer running unattended in a dry-box for long periods, agitation was effected by bubbling nitrogen through the solution. This also removed the gases formed by radiation decomposition of the solvent.

Fig. 2. shows the Perspex electrode holder.

Preparatives.—The preparations were carried out in *X*-ray capillaries of 0·4-mm. internal diameter for convenient examination of the reaction products by *X*-ray powder photography. For this purpose a simple reaction tube made in Pyrex was devised (Fig. 3). Approx. 0·2 mg. of polonium electrodeposited on a one-inch length of 0·01"-diameter gold wire was placed in the open end which was then sealed. The tube was evacuated and the polonium metal sublimed to the centre of the capillary. Volatile reactants could then be admitted and the products sealed off in the capillary for *X*-ray and subsequent chemical analysis. The outer glass tube, held on to the main stem by plasticine, protected the capillary from accidental damage.

Preparations for chemical analysis only were made in a larger version of the reaction tube with the centre capillary replaced by tubing of 4 mm. internal diameter and with the end section enlarged to 8 mm. internal diameter to accommodate foils.

The standard centrifugation technique for precipitates was not practicable for preparations of polonium compounds formed by precipitation, owing to gas-evolution and consequent scattering of the centrifuged precipitate. A form of microfilter stick was therefore devised. A fine piece of hair capillary of *ca.* 0·1 mm. internal diameter was lodged inside an open *X*-ray

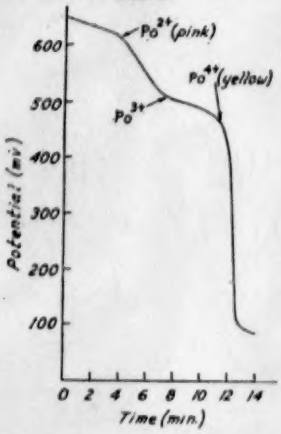
capillary which was mounted in a rubber bung held in a 15-ml. centrifuge tube. A slurry of finely powdered Pyrex glass in distilled water was then placed in the tube and centrifuged. The larger particles lodged on top of the interior tube, forming a filter pad. The finer particles which had passed through during the centrifugation were then replaced in the *X*-ray capillary and the procedure repeated in order to build up the pad. After thorough washing with distilled water the precipitation was carried out in the capillary and the precipitate centrifuged on to the filter pad. After washing and drying, the capillary was sealed off for photography.

Powder Photographs.—Samples were mounted in a 19-cm. Unicam camera and photographed, filtered Cu-$K\alpha$ radiation being used.

Analysis.—Samples for analysis were dissolved in 0·1N-nitric acid, and the chloride content estimated by potentiometric titration against 0·01N-silver nitrate solution. Titration of chloride in the presence of polonium is complicated by the tendency of the polonium to be deposited spontaneously on silver (*e.g.*, see Marckwald, *Ber.*, 1905, **38**, 591) and, at low acid concentrations, its salts are hydrolysed and are deposited on glass (*e.g.*, see Starik, *Trans. Inst. Radium, Leningrad*, 1933, **2**, 91). The addition of coagulants or indicators is also undesirable since they would complicate the recovery and estimation of the polonium.

FIG. 4.

FIG. 5.



The titration unit (Fig. 4) consisted of a silver–silver chloride and a platinum electrode, with an AgIa micrometer syringe burette. The burette had a capacity of 0·5 ml. (minimum delivery 0·002 ml.) and was fitted with a glass delivery tip into which the platinum reference electrode was sealed. Immersion of the burette tip, filled with titrant, into the solution to be titrated ensured electrical contact. To obtain a better end-point, the 1-ml. titration cell (*A*, Fig. 4) was cooled by immersion in the ice-filled jacket *B*.

Stirring was effected by rotating the cell and jacket by means of a small electric motor. All potential measurements were made on an Electronic Instruments Ltd. pH-meter. Under these conditions, control experiments with 0·01N-potassium chloride gave well-defined curves, the error in the range 30—100 μg. of chloride ion being ±0·5%.

On completion of the titration the solution was transferred to a 10-ml. graduated flask, and the cell and burette tip were washed with 2N-hydrochloric acid (10 × 0·5 ml.), the washings were combined in the flask, and the volume was made up to 10 ml. with N-nitric acid. Aliquot parts (0·01 ml.) of this solution were evaporated to dryness on glass counting trays, and the polonium content was estimated in an air ionisation chamber reading directly in the range 5 μc to 20 mc (Cuykendall and Finlayson, American report MDDC-341, 1946). In some experiments the polonium was estimated calorimetrically before the chloride estimation.

RESULTS

Electrodeposition.—The optimum applied voltage was found to lie in the range 2·0—2·2 v. Below this value the voltage tends to drift, and at higher voltages there is considerable gas evolution at the electrodes and the rate of deposition is not greatly increased.

More than 95% deposition in 4 hr. was obtained for a foil of surface area 2 $cm.^2$, but gold

wire of 0·01″ diameter (surface area 0·15 cm.²) required 16—20 hr. for the same efficiency of deposition.

Analytical.—In all calculations of the weight of polonium determined from α-counting the half-life of ^{210}Po was taken to be 138·4 days (Curtis, *Phys. Rev.*, 1953, **92**, 489). The atomic ratio of chlorine to polonium in the tetrachloride was found to be 4·06 ± 0·10 and in the dichloride 1·99 ± 0·19. The variation in the results for the dichloride is due to partial decomposition to the metal (low results) and to the presence of traces of the tetrachloride. The weight of polonium used for the analytical samples varied from 45 to 260 μg.

Polonium Tetrachloride.—The tetrachloride is a bright yellow solid, melting in chlorine (sealed tube) at about 300°. National Nuclear Energy Series, IV-19B, 1950, 256, gives m. p. 294°, b. p. 390°/1 atm.: it is not possible to determine these values with great accuracy since the temperature of the sample itself will be higher than ambient owing to the heat released in the stoppage of α-particles from the disintegration. A sealed thin-walled Pyrex tube containing 3 mg. of ^{210}Po was found to have an external temperature of 75°, the ambient temperature being 20°. The molten salt is straw-coloured up to 350°, at which temperature it becomes scarlet, and it volatilises at 400° to a purple-brown vapour. At temperatures above 500° the vapour becomes blue-green.

The tetrachloride has been prepared by dissolving metallic polonium in hydrochloric acid and slowly evaporating the solution to dryness; by heating the metal in dry chlorine; by heating the dioxide in dry hydrochloric acid or thionyl chloride vapour, or with phosphorus pentachloride. *X*-Ray results have shown that the tetrachloride is converted into the dioxide when heated in dry air or oxygen at 300° or on long storage in dry oxygen.

The tetrachloride is extremely hygroscopic and in moist halogen-free air is rapidly hydrolysed to a white solid of variable composition (chlorine : polonium ratio varying from 0·5 to 1·5) which is possibly a mixture of a basic chloride and a hydroxide or hydrated oxide. A similar result is obtained by hydrolysis of a solution of the tetrachloride in boiling water. Bouissières (*Bull. Soc. chim.*, 1952, 536), from tracer experiments, considered that this product was an oxychloride. The tetrachloride is soluble in hydrochloic acid, in water with slow hydrolysis, and in thionyl chloride, and appears to be moderately soluble in ethyl alcohol, acetone, and other ketones. With 0·1N-nitric acid it gives a white insoluble solid, containing no chlorine, which is being investigated.

Solutions in hydrochloric acid are bright yellow in concentrations as low as 5×10^{-6}M, and addition of a solution of cæsium chloride in ethyl alcohol yields a greenish-yellow precipitate of Cs_2PoCl_6, as found by Staritzky (*loc. cit.*).

Addition of ammonia or sodium hydroxide solution to solutions in dilute hydrochloric acid precipitates a buff to pale-brown flocculent solid (solubility 75 μg. of ^{210}Po per l. of water or excess of alkali). When the suspension is boiled, the precipitate becomes crystalline and yellow-brown and the solubility in excess of potassium hydroxide increases to 12 mg. of ^{210}Po per l. The precipitate, which is probably a hydrated oxide, appears to be feebly amphoteric and is being further investigated.

Reduction in Solution.—In hydrochloric acid solution the tetrachloride is reduced rapidly to the pink, bivalent state by sulphur dioxide or hydrazine in the cold and by arsenious oxide on warming. Hydroxylamine and oxalic acid have no effect, and Joliot's electrochemical observations (*loc. cit.*) on the latter may therefore be due to the formation of a complex oxalate. The reduced solutions autoxidise back to the quadrivalent state in *ca.* 480 seconds after the excess of reducing agent has been eliminated. The change of potential with time at a platinum electrode (*v.* a reference electrode) was measured in order to determine the valency state of the reduced polonium. A typical curve is shown in Fig. 5. The values of the potential given on the graph are not absolute. The break in the potential–time curve would correspond to the intermediate formation of a trichloride, but there is no other evidence for the existence of this compound.

From the time taken for the reduced state to oxidise back to the quadrivalent state, it should be possible to calculate the valency of the lower oxidation state, by assuming that the oxidation is due to the hydrogen peroxide formed in the solution under the α-bombardment from the polonium. With a *G* value of unity for the formation of hydrogen peroxide (Allen, *J. Phys. Chem.* 1948, **52**, 479), the equation $Po^{3+} + 2H^+ + H_2O_2 \longrightarrow Po^{4+} + 2H_2O$ would require 327 sec. for the complete oxidation of Po^{3+} to Po^{4+}. This time will be independent of the amount of polonium present since the polonium is itself the source of the oxidising agent. The time found (480 sec.) gives a value for the valency of the reduced state between 1 and 2, so that it is probable that the reaction is not as simple as that quoted.

However, since sulphur dioxide rapidly reduces both moist and dry solid polonium tetrachloride to the dichloride and since solutions of the dichloride in dilute hydrochloric acid give a potential–time oxidation curve identical with that obtained by reducing the tetrachloride in solution, it seems certain that the reduced solutions contain bivalent polonium.

Polonium Dichloride.—The dichloride is a dark ruby-red solid which sublimes, with some decomposition, at *ca.* 200°. National Nuclear Energy Series (*loc. cit.*) give 190° for the sublimation temperature and give the m. p. as >355°; the compound is described as a red-orange orthorhombic solid. It is prepared by careful thermal degradation of the tetrachloride at 200° in a vacuum, by reaction of sulphur dioxide with slightly moist tetrachloride in the cold, the product being dried in a stream of nitrogen, and by heating the tetrachloride in a stream of carbon monoxide or hydrogen sulphide at 150°. The reduction of tetra- to di-chloride by hydrogen sulphide and by sulphur dioxide was confirmed by *X*-ray powder photography. The dichloride is further reduced to the metal by hydrogen sulphide.

The dichloride dissolves readily in dilute hydrochloric acid to a pink solution which rapidly autoxidises to the quadrivalent state and is immediately oxidised by hydrogen peroxide or chlorine water. Addition of potassium hydroxide solution to this solution gives a dark brown precipitate (solubility 1·4 mg. of ^{210}Po/l.) which may be the hydrated bivalent oxide or hydroxide and which is very rapidly oxidised to the quadrivalent state. With 0·1N-nitric acid it gives a dark red solution and then rapidly a white flocculent precipitate, the composition of which is not known.

Polonium–Chlorine–Ammonia System.—When kept in dry ammonia gas at room temperature the tetrachloride is reduced to the metal and a trace of a compound, possibly a bivalent chloride ammine. Initially a slight orange colour was observed which could be due to the formation of an ammine of higher valency. At 100°, however, yellow $(NH_4)_2PoCl_6$ was formed. It is possible that traces of chlorine adsorbed on the walls of the reaction tube first react with the ammonia to give ammonium chloride which then combines with the polonium tetrachloride. Microgram amounts of chlorine were detected on the walls of the reaction capillary after preparation of the tetrachloride, even after evacuation to 20 μ for 30 min. Specimens of the ammonium compound were also prepared by heating polonium tetrachloride with ammonium chloride at 100° (see *X*-ray results).

At 200° polonium dichloride and tetrachloride were found by *X*-ray analysis to give an identical product, which is possibly a dichloride ammine. This is a brownish-black solid which, by analogy with tellurium (Mellor, "Comprehensive Treatise on Inorganic and Theoretical Chemistry," Longmans, Green and Co., London, 1931, Vol. XI, p. 100), might be expected to be $PoCl_2.2NH_3$.

Polonium–Chlorine–Hydrogen Sulphide System.—Solid polonium tetrachloride is reduced first to the dichloride and then to the metal when heated in dry hydrogen sulphide. Solutions of the two chlorides in hydrochloric acid yield black precipitates with hydrogen sulphide, together with much sulphur. Specimens of these precipitates gave poor *X*-ray diffraction patterns. Heating them in a vacuum gave sulphur and metallic polonium. These precipitates may be sulphides, but we have been unable to determine their composition. The system is being further investigated.

X-Ray Analysis.—(a) *Polonium dichloride.* The diffraction photographs of polonium dichloride prepared by reduction of the tetrachloride both by hydrogen sulphide and by sulphur dioxide showed no lines attributable to the oxide, metal, or tetrachloride. The observed $\sin^2\theta$ values can be indexed on the basis of an orthorhombic cell with $a = 3{\cdot}66 \pm 0{\cdot}01$, $b = 4{\cdot}34 \pm 0{\cdot}01$, and $c = 4{\cdot}49 \pm 0{\cdot}01$ kX. The agreement between the observed and calculated $\sin^2\theta$ values is seen from Table 1 to be fairly good considering the rather poor quality of the photographs. The calculated cell volume is 71·3 kX^3 which can be compatible only with one molecule of $PoCl_2$ per unit cell, giving a calculated density of 6·50 g./c.c.

TABLE 1.

hkl	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)	*I* (obs.)	*hkl*	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)	*I* (obs.)
001	0·0294	0·0294	s	012	0·1491	0·1491	m
010	0·0315	0·0315	w	021	0·1555	0·1554	vvw
100	0·0441	0·0441	w+	200	0·1769	0·1764	vw
011	0·0607	0·0609	s	210	0·2078	0·2079	vw
101	0·0726	0·0735	vw	022	0·2427	0·2436	diffuse
110	0·0751	0·0756	w	003	0·2648	0·2646	,,
111	0·1046	0·1050	w	030	0·2834	0·2835	,,
002	0·1180	0·1176	m+	013	0·2964	0·2961	,,

The observed indices of the reflections show that there are no apparent systematic absences. It appears to be rather unusual that polonium dichloride should be orthorhombic with only one molecule per unit cell. It would be more likely that this small cell was a pseudo-cell and the true cell had, for example, four times the volume. However, no extra lines attributable to a larger cell could be found.

If the small cell is really the true cell, then it should be possible to find positions for the atoms such that the observed and the calculated intensities are compatible. The space group P222 (also Pmm2 and Pmmm) requires no systematic absences and has 1- and 2-fold positions. Accordingly, with the space group D_2^1-P222, polonium was placed on the 1(*a*) position (000) and the chlorine atoms on special positions 1(*e*) and 1(*f*) ($\frac{1}{2}\frac{1}{2}0$ and $\frac{1}{2}0\frac{1}{2}$). This arrangement would give reasonable Po–Cl distances. For this space group the structure amplitude B ($= -4 \sin 2\pi hx \sin 2\pi ky \sin 2\pi lz$) is zero, as each set of atomic co-ordinates contains a zero value. It is found for the **111**, **002**, and **020** planes that, with a structure factor $A = 4 \cos 2\pi hx \cos 2\pi ky \cos 2\pi lz$, the chlorine atoms scatter completely in phase with the polonium atoms. Further, these planes are all in the same θ range (19—21°), and therefore the Lorentz polarisation correction factor and the atomic scattering factors for the atoms will be both approximately constant. Thus the calculated intensities will be proportional to the multiplicity constant p. The values of the multiplicity constant are 8, 2, and 2 for the **111**, **002**, and **020** planes respectively. The strongest plane should therefore be the 111 plane, and the other two planes should be of equal intensity. This is, in fact, not the case. The **111**, **002**, and **020** planes have the respective intensities weak, medium+, and zero. The same result is arrived at irrespective of which possible space group is used. It would appear therefore that the small orthorhombic cell is a pseudo-cell.

We are grateful to a Referee for suggesting another possibility. The dichloride might have a space group of lower symmetry, belonging to the monoclinic or even the triclinic system, but with the cell angle or angles near 90°. The single molecule might then occupy a general position.

TABLE 2.

I (obs.)	vw	w	w	w	vw	vw
$\sin^2\theta$ (obs.)	0·0098	0·0176	0·0280	0·0303	0·0381	0·0480
I (obs.)	vvw	w	vw	vvw	vvw	vvw
$\sin^2\theta$ (obs.)	0·0513	0·0625	0·0819	0·1530	0·1627	0·1716

(b) *Polonium tetrachloride.* The photographs of this compound were very poor. No lines attributable to the metal or oxide were observed. The $\sin^2\theta$ values together with the observed intensities are given in Table 2. So far it has not been possible to index the pattern owing to the rather poor values and the apparent low symmetry of the structure.

(c) *Ammonium hexachloropolonite.* The *X*-ray diffraction data showed that the product formed by treating solid polonium tetrachloride with dry ammonia and then evacuating the reaction tube was free from metallic polonium, chlorides, and dioxide. It contains, however, two phases, the major phase being face-centred cubic. From volume considerations the cell could contain four molecular units of $(NH_4)_2PoCl_6$. Polonium tetrachloride was then heated with ammonium chloride, and the product gave diffraction data identical with those of the above major phase. The existence of this compound was tentatively suggested by Guillot (*loc. cit.*) and it was prepared by Staritzky (*loc. cit.*) for optical crystallographic analysis by evaporating solutions of polonium tetrachloride and ammonium chloride in hydrochloric acid. In order to confirm the existence of this compound a complete structure analysis was carried out (Table 3).

TABLE 3.

hkl	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)	I (obs.)	I (calc.)	*hkl*	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)	I (obs.)	I (calc.)
111	0·0166	0·0166	s	100·0	422	0·1336	0·1332	w—	7·0
200	0·0220	0·0222	s—	83·4	511, 333	0·1500	0·1499	w	21·6
220	0·0440	0·0444	w	17·7					2·0
311	0·0608	0·0610	m	45·0	440	0·1776	0·1776	w—	16·6
222	—	0·0666	—	0	531	0·1941	0·1942	w—	22·6
400	0·0884	0·0888	m—	29·5	600, 442	0·1997	0·1998	w—	4·2
331	0·1056	0·1055	w	14·9					13·4
420	0·1109	0·1110	m—	36·2	620	0·2218	0·2220	vw	4·5

The agreement between the observed and the calculated values of $\sin^2\theta$ shows that the symmetry is unambiguously face-centred cubic, with the cell constant $a = 10{\cdot}33 \pm 0{\cdot}01$ kX. There are four molecules per unit cell, giving a calculated density of 2·76 g./c.c.

The compound is most probably isostructural with $(NH_4)_2PtCl_6$ (Wyckoff and Posnjak, *J. Amer. Chem. Soc.*, **1921**, **43**, 2292) which has the space group O_h^5-Fm3m with the platinum, nitrogen, and chlorine atoms on the 4(*a*), 8(*c*), and 24(*e*) special positions respectively.

Accordingly, in the present case, the same special positions were used for the polonium, nitrogen, and chlorine atoms. The variable parameter for the chlorine positions was taken as $x = 0{\cdot}23$. The contribution of the nitrogen and hydrogen atoms to the calculated intensities has been neglected as it will necessarily be swamped by the contribution from the 4 polonium and 24 chlorine atoms. It is seen from Table 3 that the agreement between the observed intensities and the calculated intensities, where $I(\text{calc.}) \propto F^2p(1 + \cos^2 2\theta)/\sin^2\theta\cos\theta$ (where F is the structure factor, p the multiplicity constant, and the function of θ is the Lorentz correction factor) is reasonably good. It appears therefore that $(NH_4)_2PoCl_6$ is isostructural with $(NH_4)_2PtCl_6$.

In this structure each polonium atom is surrounded by 8 nitrogen atoms with a Po–N distance of 4·47 kX, and by six chlorine atoms, in octahedral array, with the Po–Cl distance 2·38 kX. If this bonding is assumed to be ionic and the ionic radius of chlorine is assumed to be 1·81 kX (Pauling, "Internationale Tabellen," Vol. II, p. 611) the radius of the Po^{4+} ion is calculated to be 0·57 kX. However, it is known that the ionic Po^{4+} radius is 1·04 (Bagnall and D'Eye, *J.*, 1954, 4295), thus the Po–Cl bonding must, as would be expected, be largely covalent in character in $(NH_4)_2PoCl_6$.

This structure can be considered to be a large fluorite cell with the $PoCl_6$ ions replacing the Ca^{2+} ions and the $(NH_4)^+$ ions replacing F^- ions.

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United Kingdom Atomic Energy Authority, Research Establishment,
Harwell, Nr. Didcot, Berks. [*Received, February 8th*, 1955.]

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*Polyazabicyclic Compounds. Part I. Preliminary Experiments on the Bischler and the Bamberger Synthesis of Benzo-*1 : 2 : 4*-triazines.*

By R. A. Abramovitch and K. Schofield.

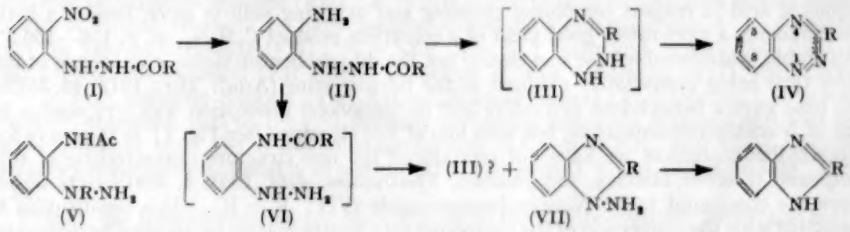
[Reprint Order No. 6130.]

(A) *N*-Acyl-*N'*-*o*-nitrophenylhydrazines have been catalytically reduced to stable *N*-acyl-*N'*-*o*-aminophenylhydrazines. Under acid conditions these amines may cyclise to dihydrobenzo-1 : 2 : 4-triazines (not isolated, but oxidised to benzo-1 : 2 : 4-triazines), or undergo acyl-group migration and subsequent cyclisation to *N*-aminobenziminazoles. The latter form benzylidene derivatives, and are oxidised by ferricyanide to benziminazoles.

(B) The cyclisation of 1 : 5-diphenyl-, 3-methyl-1 : 5-diphenyl-, and 1 : 3 : 5-triphenyl-formazan by sulphuric and acetic acid gave high yields of benzo-1 : 2 : 4-triazine, and its 3-methyl and 3-phenyl analogue, respectively. Except with the 3-phenylformazan, a methoxyl group in the potential triazine 6-position inhibits cyclisation, whilst a potential 8-methoxyl group lowers the yields. Phenazines may arise as by-products from the cyclisation of formazans with or without 3-substituents.

(A) The first synthesis of benzo-1 : 2 : 4-triazine (IV; R = H) and its 3-methyl homologue (IV; R = Me) was described by Bischler (*Ber.*, 1889, **22**, 2801), who reduced the nitrocompounds (I; R = H and Me) with sodium amalgam and alcoholic acetic acid and, without isolating either of the intermediates (II and III), oxidised the product with alkaline ferricyanide. No yields of triazines were reported, and from the reaction with the parent (I; R = H) *o*-phenylenediamine and 2-methylbenziminazole (presumably an artefact) were also obtained. The reaction with the methyl analogue (I; R = Me) also furnished a compound, m. p. 162°, regarded as the amine (II; R = Me). By similar means Bischler and Brodsky (*Ber.*, 1889, **22**, 2809) obtained 6-bromo- and 6-bromo-3-methyl-benzo-1 : 2 : 4-triazine in poor yields. In closely related experiments Hempel (*J. prakt. Chem.*, 1890, **41**,

161) claimed to have isolated benzo-1 : 2 : 4-triazine from the action of cold phosphoric anhydride upon the hydrazine (V; R = Me or Et).



A few attempts which we made to prepare benzo-1 : 2 : 4-triazine by Bischler's method were discouraging, reduction of the nitro-compound being far from complete (reduction must also have been incomplete in Bischler's own experiments, since the reduction product gave in alkali a dark blue-violet colour which disappeared suddenly during subsequent oxidation, and the acylnitrophenylhydrazines all give deeply coloured solutions in alkali, as Bischler himself reported). Accordingly, the catalytic reduction of *N*-formyl-, *N*-acetyl-, and *N*-benzoyl-*N'*-*o*-nitrophenylhydrazine was examined. In warm ethanol, in the presence of palladium–charcoal, reduction was rapid and quantitative. The colourless reduced solutions became yellow in air, and fresh alcohol produced pink or red colorations, but careful concentration retrieved high yields of the amines (II; R = H, Me, or Ph) as colourless crystalline solids. (It is assumed that under the conditions of preparation acyl-group migration would not occur, but at present formal proof of the presence of an amine group is lacking. On treatment with nitrous acid the compounds gave solutions which with alkaline β-naphthol merely formed yellow precipitates.) Unlike the nitro-compounds these amines were, as expected, insoluble in alkali, and it is interesting that *N*-acetyl-*N'*-*o*-aminophenylhydrazine had substantially the same m. p. (164—166°) as the by-product assigned this structure by Bischler (*loc. cit.*).

The amines were quite stable under ordinary conditions and specimens have been kept unchanged for several months. On one occasion only was different behaviour observed; a specimen of *N*-formyl-*N'*-*o*-aminophenylhydrazine, several months old, had changed to a tar from which light petroleum extracted *ca.* 45% of benzo-1 : 2 : 4-triazine. This behaviour has not been observed again despite attempts to stimulate it, and consequently the amines were submitted to various conditions which might be expected to effect cyclisation.

For the formally analogous conversion of acyl derivatives of *o*-phenylenediamine into benziminazoles, 4N-hydrochloric acid is a convenient reagent (Phillips, *J.*, 1928, 172). The colourless solutions of *N*-*o*-aminophenyl-*N'*-formylhydrazine in this acid quickly became deep red when heated. Basification destroyed the colour, and oxidation of the resulting mixture with potassium ferricyanide produced benzo-1 : 2 : 4-triazine. The low yield (10—20%) appeared to decrease slightly if heating of the amine with acid was prolonged, and the triazine appeared to be accompanied by a colourless by-product. Most of the starting material remained unaccounted for. *N*-Acetyl-*N'*-*o*-aminophenylhydrazine behaved similarly, but in this instance oxidation produced good yields of 3-methylbenzo-1 : 2 : 4-triazine, which again fell when the initial step was prolonged. From this reaction 2-methylbenziminazole was also isolated. *N*-*o*-Aminophenyl-*N'*-benzoylhydrazine, treated for a short time with hot hydrochloric acid, behaved similarly to its analogues, and subsequent oxidation led to the formation of 3-phenylbenzo-1 : 2 : 4-triazine (22%); however, on prolonged warming of the amine with acid there separated from the initially deep-red solution a dark oil. This was probably the dihydrobenzotriazine, for it slowly deposited the yellow triazine which was then isolated in improved yield (37%). From both experiments with the benzoyl compound small amounts of a colourless by-product, m. p. 204—205°, were isolated, identical with that discussed below.

When cyclisation and oxidation were attempted with nitrobenzene in benzene saturated with hydrogen chloride, *N-o*-aminophenyl-*N'*-formylhydrazine gave a low yield of benzo-1 : 2 : 4-triazine, but the same amine boiled with an aqueous solution of *m*-nitrobenzenesulphonic acid (a reagent combining cyclising and oxidising ability) gave, besides a little benzotriazine, a moderately good yield of a colourless product $C_7H_7N_3$, m. p. 156—156·5°. This stable, water-soluble base was clearly not the dihydrobenzotriazine, compounds of the latter type being immediately oxidised to the benzotriazine (Arndt, *Ber.*, 1913, **46**, 3522). The base gave a benzylidene derivative and its ultraviolet absorption was very similar to that of *N*-methylbenziminazole, but with loss of fine structure [see Fig. 1; in the curve for *N*-methylbenziminazole we have not reproduced the fine structure characteristic of this compound (Beaven, Holiday, and Johnson, *Spectrochim. Acta*, 1951, **4**, 338)], facts which prove the compound to be *N*-aminobenziminazole (VII; R = H). This constitution is consistent with the conversion of the compound into benziminazole by alkaline ferricyanide, a reaction analogous to the oxidation of *N*-methyl-*N*-phenylhydrazine to methylaniline by Fehling's solution (Fischer, *Annalen*, 1878, **190**, 167). (The reaction also accounts for the

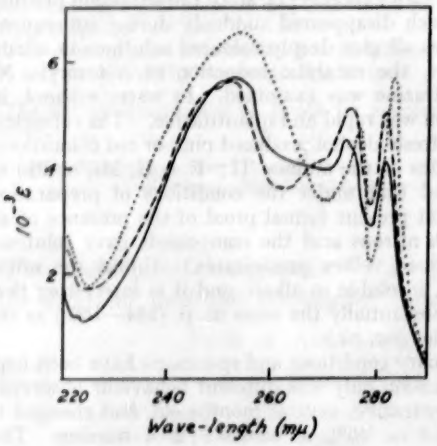


FIG. 1. *Absorption spectra of* (——) 1-*amino-benziminazole* (*in* EtOH), (– – –) 1-*Amino-2-methylbenziminazole* (*in* EtOH), *and* (. . .) N-*methylbenziminazole* (*in hexane*) (Beavan *et al.*, *loc. cit.*).

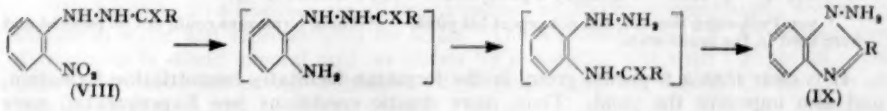
isolation of 2-methylbenziminazole in the experiments discussed above.) That an oxidising agent other than atmospheric oxygen is unnecessary for the formation for benzo-1 : 2 : 4-triazine was shown by the formation of a moderate yield of this compound, together with *N*-aminobenziminazole, when the hydrazide (II; R = H) was heated in benzene solution with a cation-exchange resin.

The acetyl and the benzoyl derivative (II; R = Me and Ph) likewise, with aqueous *m*-nitrobenzenesulphonic acid, gave 1-amino-2-methyl- (VII; R = Me) and 1-amino-2-phenyl-benziminazole (VII; R = Ph) (identical with the compound mentioned above), as well as low yields of the benzotriazines. 1-Amino-2-methylbenziminazole was characterised by its ultra-violet absorption spectrum (Fig. 1), by conversion into a benzylidene derivative, and by oxidation to 2-methylbenziminazole.

The formation of *N*-aminobenziminazoles must involve acyl-group migration from the hydrazine to the amine nitrogen atom (II ⟶ VI), followed by preferential formation of the five-membered ring (VI ⟶ VII). Whether the small concomitant yields of benzo-1 : 2 : 4-triazines arise from the acylamino-compound (VI ⟶ III), or from the acylhydrazine (II ⟶ III) is not established. The preferential formation of a five-membered ring recalls the formation of *N*-amino-oxindole from *o*-hydrazinophenylacetic acid (Neber, *Ber.*, 1922, **55**, 826). Acyl-group migrations are not uncommon (see Theilacker, "Isomerisation," in Schwab's "Handbuch der Katalyse," 1943, Vol. VII, 302, Springer, Vienna), but migration from a hydrazino- to an amino-group seems not to have been recognised

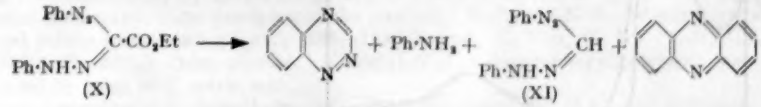
before. Guha and Ghosh (*J. Indian Chem. Soc.*, 1928, **5**, 439) claimed to have obtained stable 3-aminodihydrobenzo-1 : 2 : 4-triazine by reducing *o*-nitrophenylsemicarbazide or *o*-nitrophenylthiosemicarbazide (VIII; R = NH_2, X = O or S) with tin and boiling hydrochloric acid, and similarly to have isolated dihydro-3-methylthiobenzo-1 : 2 : 4-triazine from the thiosemicarbazide (VIII; R = SMe, X = S). Guha and Arndt (*ibid.*, 1931, **8**, 199) subsequently showed that careful reduction of this compound (VIII; R = NH_2, X = S) with stannous chloride gave, instead, 3-aminobenzo-1 : 2 : 4-triazine. It is very probable, therefore, that in the first instance acyl-group migration occurred and that the stable products were the *N*-aminobenziminazoles (IX; R = NH_2 and SMe). Similar remarks are probably applicable to certain other compounds (Guha and Ray, *ibid.*, 1925, **2**, 83).

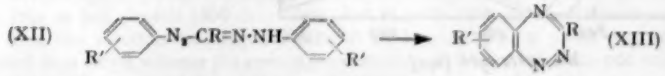
Finally, the Bischler reaction has been applied to the readily available formyl and acetyl derivatives of 2 : 4-dinitrophenylhydrazine. Reduction of both nitro-groups in the



formyl compound was readily effected with hydrogen and palladium–charcoal, but the colourless reduced solution rapidly became deep orange-red in the atmosphere, and on concentration gave 6-aminobenzo-1 : 2 : 4-triazine in low yield. The acetyl derivative similarly gave 6-amino-3-methylbenzo-1 : 2 : 4-triazine. Various attempts were made to improve the yields of these products: hydrogenation in alcohol containing hydrochloric acid caused no improvement, and in acetic acid saturated with hydrogen chloride was very slow owing to the formation of an insoluble hydrochloride; a cation-exchange resin also failed to improve the process.

(B) An alternative synthesis of benzo-1 : 2 : 4-triazine was reported by Bamberger and Wheelwright (*Ber.*, 1892, **25**, 3201), who obtained it together with aniline, 1 : 5-diphenylformazan (XI), and phenazine by the action of hot concentrated mineral acids on 3-ethoxycarbonyl-1 : 5-diphenylformazan (X), the triazine probably arising from the 1 : 5-diphenylformazan formed by hydrolysis and decarboxylation.





Similarly the formazans (XII; R = Ac and Bz; R′ = H) gave good yields of the corresponding benzotriazines (XIII; R = Ac and Bz; R′ = H), but unaccompanied by phenazines (Bamberger and Lorenzen, *Ber.*, 1892, **25**, 3539; Bamberger and Witter, *Ber.*, 1893, **26**, 2788). The course of the reaction is influenced by the nature of R. Thus benzotriazine formation occurred with the compounds (XII; R = Ph, *o*-C_6H_4·OH, or 3 : 4-CH_2O_2:C_6H_4; R′ = H) (von Pechmann, *Ber.*, 1894, **27**, 1679; Fichter and Fröhlich, *Brit. Abs.*, 1903, **84**, 722), but different products arose from the analogues (XII; R = NO_2, NH_2, or Cl; R′ = H) (Bamberger, Padova, and Ormerod, *Annalen*, 1925, **446**, 260; Fusco and Romani, *Gazzetta*, 1946, **76**, 419). The unsymmetrical 3 : 5-diphenyl-1-*p*-tolyl- (von Pechmann, *loc. cit.*), 3 : 5-diphenyl-1-*p*-sulphonophenyl- (Fichter and Schiess, *Ber.*, 1900, **33**, 747), and 1-α-naphthyl-3 : 5-diphenyl-formazan (*idem*, *loc. cit.*) were cyclised to 6-methyl-3-phenyl- and 3-phenyl-benzo-1 : 2 : 4-triazine and 3-phenylnaphtho(2′ : 1′-5 : 6)-1 : 2 : 4-triazine respectively. Further examples were reported by Massini (*Ann. Chim. farm.*, 1940, 24) and Parkes and Aldis (*J.*, 1938, 1841).

We have examined selected examples of this cyclisation with the aim of establishing its efficiency, and of further defining the effect of substituents in the formazan upon the reaction. The results of heating the nine symmetrical formazans (XII; R = H, Me, or Ph; R′ = H, *o*-OMe, or *p*-OMe) with concentrated sulphuric and glacial acetic acid are summarised below.

Formazan (XII)	Product.
R = R′ = H	Benzo-1 : 2 : 4-triazine (61%), phenazine (3·5%)
R = Me, R′ = H	3-Methylbenzo-1 : 2 : 4-triazine (70%)
R = Ph, R′ = H	3-Phenylbenzo-1 : 2 : 4-triazine (87%) [1]
R = H, R′ = *o*-OMe	8-Methoxybenzo-1 : 2 : 4-triazine (38·5%), 1 : 6-dimethoxyphenazine (3·8%)
R = Me, R′ = *o*-OMe	8-Methoxy-3-methylbenzo-1 : 2 : 4-triazine (39·3%), 1 : 6-dimethoxyphenazine (8·3%)
R = Ph, R′ = *o*-OMe [2]	8-Methoxy-3-phenylbenzo-1 : 2 : 4-triazine (43%)
R = H, R′ = *p*-OMe...	Possibly a trace of 2 : 7-dimethoxyphenazine
R = Me, R′ = *p*-OMe [2]	No product isolated
R = Ph, R′ = *p*-OMe	6-Methoxy-3-phenylbenzo-1 : 2 : 4-triazine (30%)

[1] von Pechmann (*loc. cit.*) did not report his yield. [2] These formazans could not be purified and were used in the crude state.

It is clear that a *C*-phenyl group in the formazan facilitates benzotriazine formation, and also improves the yield. Thus, more drastic conditions (see Experimental) were

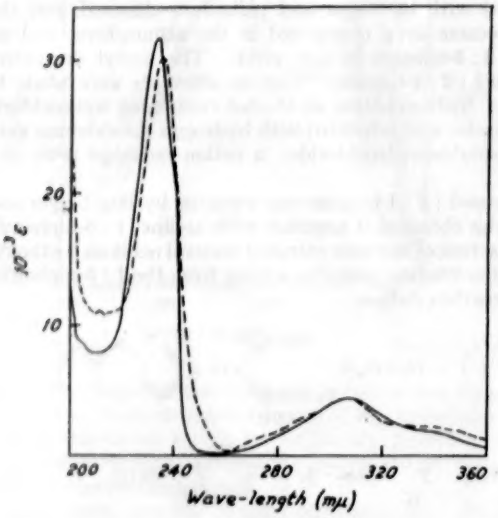


FIG. 2. *Absorption spectra of* (——) *benzo-*1 : 2 : 4*-triazine* (*in* H_2O) *and* (– – –) 3*-methyl-*1 : 2 : 4*-triazine* (*in* H_2O).

necessary with 3-unsubstituted formazans than with 3-methyl- or 3-phenyl-formazans. Phenazine formation can occur with both 3-unsubstituted and 3-substituted formazans, and the production of 1 : 6-dimethoxyphenazine from 1 : 5-di-*o*-methoxyphenyl-3-methylformazan indicates that only the 1 : 5-substituents in the formazans are involved in phenazine formation. Whilst the effects of substituents accord with the obvious nature of the process of triazine formation as an electrophilic substitution into the benzene ring, the nature of the reaction leading to phenazines is not clear [the scheme outlined by Bamberger and Wheelwright (*loc. cit.*) cannot be seriously considered]. A methoxyl group situated *meta* to the point of cyclisation is detrimental to the reaction, lowering the yield or completely preventing triazine formation. Such an effect is frequently observed in electrophilic cyclisations such as the Combes quinoline synthesis (Roberts and Turner, *J.*, 1927, 1832), the Sandmeyer isatin synthesis (Halberkann, *Ber.*, 1921, **54**, 3079; Theobald, Thesis, London, 1949), and various reactions in the carbocylic series (Hey and Kohn, *J.*, 1949, 3177; Hey and Nagdy, *J.*, 1953, 1894).

Our evaluation of the two methods shows that in general the Bamberger synthesis is superior for the production of benzo-1 : 2 : 4-triazines to the Bischler synthesis, except when the inhibiting effect of a potential 6-methoxyl group is not counterbalanced by a suitable 3-substituent. This conclusion is strengthened by the difficult accessibility of hydrazines suitable for the Bischler reaction.

Attempts to demethylate 8-methoxy-, 8-methoxy-3-methyl-, and 8-methoxy-3-phenylbenzo-1 : 2 : 4-triazine with aluminium chloride in benzene gave phenolic products which appeared from analysis to contain either benzene of crystallisation or to have been substituted by a phenyl group, the figures favouring the second possibility. The method of purification (vacuum-sublimation) rendered unlikely the retention of solvent of crystallisation, and the tentative formulation of these compounds as phenylated 8-hydroxybenzo-1 : 2 : 4-triazines is further supported by molecular-weight (Rast) determination. We have found no analogy for phenylation under these conditions, and are further examining these compounds.

The benzo-1 : 2 : 4-triazines are all bright yellow, weakly basic compounds, noticeably soluble in water and reprecipitated by alkali. The 6-aminobenzo-1 : 2 : 4-triazines were diazotisable in dilute mineral acid, as shown by a coupling test with β-naphthol. The ultraviolet extinction curves of benzo-1 : 2 : 4-triazine and the 3-methyl derivative are reproduced (Fig. 2).

Experimental

(A) *The Bischler Synthesis*

N-*Acyl*-N′-o-*nitrophenylhydrazines*.—*o*-Nitrophenylhydrazine (7 g.) and 100% formic acid (7 c.c.) were heated at 95° for 1 hr. Removal of the solvent and crystallisation of the residue from alcohol gave mustard-yellow crystals of the product (7·9 g.), m. p. 181—182°. Similarly the hydrazine (5 g.), acetic acid (10 c.c.), and fused sodium acetate (0·5 g.) gave the acetyl derivative which formed golden needles (4·9 g.), m. p. 142—144°, from alcohol. *o*-Nitrophenylhydrazine (5 g.), benzoyl chloride (4·75 g.), and pyridine (30 c.c.), kept overnight at room temperature, and then heated 1½ hr. at 95°, gave when poured into iced dilute hydrochloric acid a gum which slowly solidified. Recrystallisation from alcohol (charcoal) gave bright yellow crystals of the benzoyl derivative (4 g.), m. p. 163—165°. Each of these derivatives dissolved in aqueous sodium hydroxide to give a permanganate-coloured solution.

2 : 4-Dinitrophenylhydrazine (10 g.) and 90% formic acid (50 c.c.), boiled for 18 hr., gave a solution from which water precipitated the product. N-*Formyl*-N′-2 : 4-*dinitrophenylhydrazine* formed yellow needles (9·5 g.), m. p. 187—188° (Found : C, 37·0; H, 2·6. $C_7H_4O_5N_4$ requires C, 37·2; H, 2·7%), from alcohol. *N*-Acetyl-*N*′-2 : 4-dinitrophenylhydrazine was similarly prepared by using 90% acetic acid.

N-o-*Aminophenyl*-N′-*formylhydrazine*.—The nitro-compound (3 g.) and palladium–charcoal (1·2 g. of 5%) in hot alcohol (300 c.c.) were shaken with hydrogen. Reduction was complete in ¼ hr., then the solution was rapidly filtered (it became yellow when exposed to air) and concentrated to a small volume (to ensure good recovery concentration in one stage to as small a volume as possible is essential) in a stream of nitrogen, under reduced pressure. After cooling, the product (1·9 g.) was collected. The *amine* formed soft needles, m. p. 120—121° (Found : C, 55·1; H, 5·6; N, 27·7. $C_7H_9ON_3$ requires C, 55·6; H, 6·0; N, 27·8%). It gave no diazonium reaction and was insoluble in alkali.

N-*Acetyl*-N′-o-*aminophenylhydrazine*.—The nitro-compound (5 g.) in hot alcohol (500 c.c.) was reduced as above. Washing with alcohol produced a pink colour in the initially colourless reduction solution, and the whole became orange before concentration, which, effected as above, gave a white solid (3·6 g.). The *amine* formed crisp rods, m. p. 164—166° (with some bubbling) (Found : C, 58·3; H, 6·7; N, 25·2. $C_8H_{11}ON_3$ requires C, 58·2; H, 6·7; N, 25·4%), from alcohol.

N-o-*Aminophenyl*-N′-*benzoylhydrazine*.—The nitro-compound (3·9 g.), catalyst (1·5 g.), and alcohol (150 c.c.), reduced as above, gave a solution which became burgundy-red when diluted with alcohol. The colour disappeared during concentration, and the *product* (2·5 g.) formed silky needles, m. p. 163—164° (Found : C, 68·9; H, 5·8. $C_{13}H_{13}ON_3$ requires C, 68·7; H, 5·8%), from ethyl acetate.

Experiments with N-o-*Aminophenyl*-N′-*formylhydrazine*.—(i) The amine (0·39 g.) and 4N-

hydrochloric acid (4 c.c.) gave a hydrochloride which quickly dissolved on warming. At 95° the initially colourless solution rapidly became deep red, and after 6 min. at this temperature it was stirred into iced water (16 c.c.) containing potassium hydroxide (3·5 g.). Addition of potassium ferricyanide (1·7 g.) in water (16 c.c.) caused a small rise in temperature and produced a flocculent black precipitate with some effervescence. After 15 min. the mixture was extracted continuously with ether for several hr. Removal of the ether gave a black oil (0·28 g.) which was digested with light petroleum (100 c.c.; b. p. 40—60°). The turbid yellow extract deposited a very small quantity of white needles, m. p. 116—117°, when cool, and the solution, when passed over alumina, gave a yellow band which on elution with benzene provided benzo-1 : 2 : 4-triazine (60 mg.). The pure compound formed deep yellow plates, m. p. 76—77° (Found : C, 64·2; H, 4·1. Calc. for $C_7H_5N_3$: C, 64·1; H, 3·8%) [$\lambda_{max.}$ (in H_2O) 233, 307 mμ; 10^{-3} ε 31·7, 4·25], after sublimation (80°/1 mm.) and recrystallisation from light petroleum. Bischler (*loc. cit.*) gave m. p. 65—66°, whereas Bamberger and Wheelwright (*loc. cit.*) gave m. p. 74—75°. The picrate separated very slowly from alcohol as brown prisms, m. p. 98—99° after sintering at 87°, which decomposed into the components on attempted recrystallisation.

From an experiment precisely similar, except that heating at 95° was continued for ½ hr., a sticky dark brown solid (0·15 g.) was obtained which yielded benzo-1 : 2 : 4-triazine (40 mg.) by chromatography, and a brown, light petroleum-insoluble solid (50 mg.).

(ii) The amine (0·4 g.), nitrobenzene (5 drops), and benzene (20 c.c.) saturated with hydrogen chloride, were refluxed for 2 hr. The colourless liquid became yellow and deposited a dark-red oil. Water was added, the aqueous layer was extracted with benzene, and the combined extracts were concentrated, diluted with light petroleum, and treated with hydrogen chloride. The precipitate was washed with light petroleum saturated with hydrogen chloride, treated with water, and extracted with benzene. Evaporation of the benzene and addition of light petroleum gave benzo-1 : 2 :4-triazine (70 mg.), m. p. 73—74°.

(iii) The amine (0·2 g.) and an aqueous solution of sodium *m*-nitrobenzenesulphonate (0·33 g.) which had been made just acid to litmus with dilute hydrochloric acid were refluxed for 1 hr. The solid dissolved quickly and the solution became deep orange-yellow (or deep red in larger runs). When cool it was strongly basified with sodium hydroxide solution and extracted continuously with benzene. Concentration of the extract and addition of light petroleum (b. p. 60—80°) gave white plates which were repeatedly washed with hot light petroleum. The combined filtrates (A) were preserved. Crystallised from benzene (charcoal) the solid gave shiny plates (110 mg.) of 1-*aminobenziminazole*, m. p. 156—156·5° (Found : C, 63·2; H, 5·2; N, 32·0; *M*, 133. $C_7H_7N_3$ requires C, 63·1; H, 5·3; N, 31·6%; *M*, 131) [$\lambda_{max.}$ (in EtOH) 252, 274, 282 mμ; 10^{-3} ε 5·67, 4·50, 4·10; $\lambda_{min.}$ 224, 270, 279, mμ; 10^{-3} ε 1·09, 3·95, 2·90]. This compound (0·1 g.), benzaldehyde (0·1 c.c.), ethyl alcohol (2 c.c.), and piperidine (1 drop) were refluxed for 1 hr. Dilution with water and trituration of the oil gave a solid (0·12 g.). 1-*Benzylideneaminobenziminazole* formed small needles, m. p. 126—127° (Found : C, 76·2; H, 4·9; N, 18·8. $C_{14}H_{11}N_3$ requires C, 76·0; H, 5·0; N, 19·0%), from ligroin containing a little benzene.

The filtrates (A), when concentrated and passed over alumina, yielded benzo-1 : 2 : 4-triazine (45 mg.), m. p. 73—74°.

(iv) The amine (0·2 g.) in benzene (20 c.c.) was refluxed overnight with Amberlite IR-120(H) (0·2 g.). Filtration, concentration, and addition of light petroleum gave 1-aminobenziminazole (0·04 g.), m. p. 151—152°. Chromatography of the remaining solution over alumina gave benzo-1 : 2 : 4-triazine (0·07 g.), m. p. 73—74°.

Oxidation of 1-*Aminobenziminazole*.—The compound (0·4 g.) in 4N-hydrochloric acid (4 c.c.) was heated at 95° for 6 min. Pouring the solution into iced water (16 c.c.) containing potassium hydroxide (3·5 g.) precipitated starting material (m. p. and mixed m. p.). Addition of an ice-cold solution of potassium ferricyanide (1·7 g.) in water (16 c.c.) produced effervescence and mild frothing, and during 15 min., with occasional shaking, the solid gradually dissolved and the solution darkened. Continuous extraction with benzene, followed by concentration of the extract and addition of light petroleum, gave a colourless precipitate. Recrystallisation from water provided benziminazole (0·18 g.), m. p. and mixed m. p. 170—171° [picrate, m. p. and mixed m. p. 225—226°].

Experiments with N-*Acetyl*-N′-*o-aminophenylhydrazine*.—(i) The amine (1 g.) dissolved immediately in 4N-hydrochloric acid (10 c.c.), and the pale yellow solution when warmed at 95° quickly become deep red. After 5 minutes' heating, the solution was poured into iced water (40 c.c.) containing potassium hydroxide (9 g.). Potassium ferricyanide (4 g.) in water (40 c.c.) was added, and after being occasionally shaken during 15 min. at room temperature, the mixture was extracted continuously with benzene. Removal of the solvent gave a brown solid (0·62 g.)

which was extracted with boiling light petroleum (100 c.c.). The extract gave by passage over alumina 3-methylbenzo-1 : 2 : 4-triazine (0·5 g., 56·8%), m. p. 92—94°. This formed bright-yellow rods, m. p. 97—98° (Found : C, 66·2; H, 4·8; N, 28·9. Calc. for $C_8H_7N_3$: C, 66·2; H, 4·9; N, 28·95%) [$\lambda_{max.}$ (in H_2O) : 235, 307 mμ; $10^{-3}\varepsilon$ 30·5, 4·30], from light petroleum. Bischler (*loc. cit.*) gave m. p. 88—89°. The petroleum-insoluble residue (0·13 g.) gave needles of 2-methylbenziminazole, m. p. and mixed m. p. 173—174° (Found : C, 72·4; H, 6·0. Calc. for $C_8H_8N_2$: C, 72·7; H, 6·1%), from benzene.

A similar experiment with heating for ½ hr. gave 34 mg. of 3-methylbenzo-1 : 2 : 4-triazine and 60 mg. of by-product. Heating for 10 min. gave 40% of the triazine.

(ii) The amine (0·2 g.), nitrobenzene (5 drops), and toluene (20 c.c.) saturated with hydrogen chloride were refluxed for 1 hr. (In the absence of acid no cyclisation occurred.) Worked up as in the experiment with the formyl compound the solution yielded 3-methylbenzo-1 : 2 : 4-triazine (80 mg.), m. p. 97—98°.

(iii) The amine (0·2 g.) and a slightly acidified solution of sodium *m*-nitrobenzenesulphonate (0·33 g.) in water (10 c.c.) were refluxed for 2 hr. Basification and continuous extraction of the solution with benzene, concentration, and addition of light petroleum, gave *1-amino-2-methylbenziminazole* (0·11 g.) which formed leaflets, m. p. 164—165° (Found : C, 57·3; H, 6·55; N, 28·5%; *M*, 159. $C_8H_9N_3,H_2O$ requires C, 58·2; H, 6·7; N, 25·4%; *M*, 165) [$\lambda_{max.}$ (in EtOH) 252, 275, 282 mμ; $10^{-3}\varepsilon$ 5·60, 5·10, 5·00; $\lambda_{min.}$ 224, 263, 279 mμ; $10^{-3}\varepsilon$ 1·70, 3·59, 3·30], from benzene (the m. p. was depressed on admixture with starting material). The *benzylidene* derivative, formed as in the previous case, gave needles, m. p. 133·5—134·5° (Found : C, 76·1; H, 5·5; N, 17·9. $C_{15}H_{13}N_3$ requires C, 76·6; H, 5·6; N, 17·9%), from benzene–ligroin.

Chromatography of the filtrate remaining after removal of the aminobenziminazole gave 3-methylbenzo-1 : 2 : 4-triazine (40 mg.), m. p. 94—95°.

Oxidation of 1-Amino-2-methylbenziminazole.—The amine (0·6 g.), suspended in water (32 c.c.) containing potassium hydroxide (7 g.), was treated at 0° with potassium ferricyanide (3·4 g.) in water (32 c.c.). Evolution of nitrogen was slow and a flocculent precipitate was formed as the amine dissolved. After 1 hr. the dark suspension was extracted continuously with benzene. Evaporation of the solvent and crystallisation of the residue from water gave 2-methylbenziminazole (0·28 g.), m. p. and mixed m. p. 174—176°.

Experiments with N-o-Aminophenyl-N′-benzoylhydrazine.—(i) The amine (0·5 g.) and 4N-hydrochloric acid (5 c.c.) were heated at 95° for 6 min. The resulting clear red solution was poured into iced water (200 c.c.) containing potassium hydroxide (4·1 g.). The addition of potassium ferricyanide (1·41 g.) in water (15 c.c.) immediately produced a dull red colour, and a dark brown precipitate was slowly formed. After 15 min. the mixture was extracted continuously with benzene. The concentrated (5 c.c.) extract deposited crystals (60 mg.), m. p. 198—200°, identical with the aminobenziminazole described below, and the remaining solution gave, by passage over alumina, 3-phenylbenzo-1 : 2 : 4-triazine (100 mg.), which formed yellow prisms, m. p. 126—127° (Found : C, 75·6; H, 4·4. Calc. for $C_{13}H_9N_3$: C, 75·3 : H, 4·4%), from benzene–light petroleum. von Pechmann (*loc. cit.*) gave m. p. 123°.

(ii) When the amine (0·2 g.) was refluxed for 2 hr. with nitrobenzene (6 drops) and toluene (20 c.c.) saturated with dry hydrogen chloride, and the solution was decanted from the oily hydrochloride which was then treated as before, finally by passage of the benzene extract over alumina and elution with benzene–ether (1 : 1), 3-phenylbenzo-1 : 2 : 4-triazine (70 mg.), m. p. 126—127°, was obtained.

(iii) Treatment of the amine (0·2 g.) as before with a slightly acidified solution of sodium *m*-nitrobenzenesulphonate (0·4 g.) in water (10 c.c.) and addition of light petroleum to the final extract gave *1-amino-2-phenylbenziminazole* (100 mg.), m. p. 204—205° (Found : C, 74·7; H, 5·35. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3%), after fractional crystallisation from benzene to remove a trace of a colourless powder.

The initial filtrate afforded by chromatography 3-phenylbenzo-1 : 2 : 4-triazine (50 mg.), m. p. 123—124°.

6-Aminobenzo-1 : 2 : 4-triazine.—Hydrogenation of *N*-2 : 4-dinitrophenyl-*N′*-formylhydrazine (2 g.) in hot ethanol (300 c.c.) in the presence of palladium–charcoal (2 g. of 5%) was complete in 20 min. After filtration, the combined filtrate and washings, which gradually became orange-red, were evaporated to small bulk, brown crystals (220 mg.) separating. After sublimation (200°/1 mm.) and recrystallisation from ethanol, this gave shiny golden platelets of *6-aminobenzo-1 : 2 : 4-triazine*, m. p. 298—299° (decomp.) (Found : C, 57·9; H, 4·1; N, 38·0. $C_7H_6N_4$ requires C, 57·5; H, 4·1; N, 38·4%). In a diazonium coupling test with alkaline β-naphthol this gave a deep violet dye.

6-Amino-3-methylbenzo-1 : 2 : 4-triazine.—In the same way *N*-acetyl-*N'*-2 : 4-dinitrophenylhydrazine (2 g.) gave golden-yellow needles (200 mg.) of *6-amino-3-methylbenzo-1 : 2 : 4-triazine*, m. p. 265—266° (decomp.) (Found : C, 59·4; H, 5·4. $C_8H_8N_4$ requires C, 60·0; H, 5·0%).

(B) *The Bamberger Synthesis*

Benzo-1 : 2 : 4-triazine.—A solution of 1 : 5-diphenylformazan (5 g.) (von Pechmann, *loc. cit.*) in acetic acid (75 c.c.) was treated slowly at 0° with concentrated sulphuric acid (20 c.c.). The violet solution was unchanged by heating for 4 min. at 95° and more sulphuric acid (10 c.c.) was then added. After a further ¼ hr. at 95° the colour had changed to yellowish-brown, and after dilution with water (200 c.c.) the mixture was extracted continuously with benzene. Concentration of the extract to a small volume, addition of light petroleum, passage over alumina (6″ × 1″), and elution with benzene–light petroleum (1 : 1) gave, first, phenazine (0·14 g.) [yellow prisms, m. p. and mixed m. p. with a specimen prepared by the method of Waterman and Vivian (*J. Org. Chem.*, 1949, **14**, 289), 176—177° (Found : C, 80·2; H, 4·5. Calc. for $C_{12}H_8N_2$: C, 80·0; H, 4·5%), from alcohol], and then benzo-1 : 2 : 4-triazine (1·65 g.), m. p. 76—77° after recrystallisation from light petroleum.

3-Methylbenzo-1 : 2 : 4-triazine.—The mauve solution of 3-methyl-1 : 5-diphenylformazan (0·4 g.) (Bamberger and Müller, *J. prakt. Chem.*, 1901, **64**, 213) in acetic acid (6 c.c.) became deep blue on the addition at 0° of concentrated sulphuric acid (1·6 c.c.), and then dark greenish-brown after 2 min. at 95°. Diluted and worked up as before this solution yielded 3-methylbenzo-1 : 2 : 4-triazine (0·17 g.).

3-Phenylbenzo-1 : 2 : 4-triazine.—1 : 3 : 5-Triphenylformazan (2 g.) (Ashley, Davis, Nineham, and Stock, *J.*, 1953, 3881) with glacial acetic acid (30 c.c.) and concentrated sulphuric acid (8 c.c.) (10 minutes' heating; the colour changed in 1 min.) behaved similarly to the methyl compound, and chromatography followed by sublimation afforded 3-phenylbenzo-1 : 2 : 4-triazine (1·2 g.).

1 : 5-Di-o-methoxyphenylformazan.—A diazonium solution prepared from *o*-anisidine (31 g.), concentrated hydrochloric acid (48 c.c.), and water (30 c.c.), and sodium nitrite (18 g.) in water (30 c.c.) was added to a solution of malonic acid (26 g.) and sodium acetate (50 g.; hydrated) in water (400 c.c.), stirred at 0°. After 10 min. sodium acetate (50 g.) was added and the solution was kept at 0° overnight (considerable frothing occurred). The precipitate was washed with water and a little methanol, and finally crystallised from ethanol. *1 : 5-Di-o-methoxyphenylformazan* (24 g.) was obtained as maroon blades, m. p. 151—152° (Found : C, 63·1; H, 5·5. $C_{15}H_{16}O_2N_4$ requires C, 63·4; H, 5·7%).

8-Methoxybenzo-1 : 2 : 4-triazine.—The deep blue solution of 1 : 5-di-*o*-methoxyphenylformazan (10 g.), acetic acid (150 c.c.), and concentrated sulphuric acid (60 c.c.) became dark brown in 15 min. at 95°. After a total of 45 minutes' heating it was diluted with water (300 c.c.) and worked up as before. Elution from the alumina column with benzene gave a mixture from which *8-methoxybenzo-1 : 2 : 4-triazine* (2·20 g.) [deep-yellow plates, m. p. 149—150° (Found : 60·2; H, 4·5. $C_8H_7ON_3$ requires C, 59·6; H, 4·4%), from benzene–light petroleum] sublimed at 150°/1 mm., leaving a residue which on crystallisation from alcohol provided yellow needles of 1 : 6-dimethoxyphenazine, m. p. 253—254° (Found : C, 69·7; H, 4·8. Calc. for $C_{14}H_{12}O_2N_2$: C, 70·0; H, 5·0%). Yoshioka and Kidani (*J. Pharm. Soc. Japan*, 1952, **72**, 847) gave m. p. 251°. The phenazine exhibits a characteristic green fluorescence in dilute alcoholic solution.

1 : 5-Di-o-methoxyphenyl-3-methylformazan.—The diazonium solution from *o*-anisidine (1·5 g.), concentrated hydrochloric acid (2·6 c.c.), water (4 c.c.), and sodium nitrite (0·9 g.) in water (2 c.c.) was added to potassium hydroxide (5·5 g.) in water (55 c.c.) at 0°. This solution was added portionwise to a vigorously stirred solution of pyruvic acid *o*-methoxyphenylhydrazone (5·2 g.) [prepared from pyruvic acid and *o*-methoxyphenylhydrazine hydrochloride in water, this *hydrazone* formed yellow prisms, m. p. 119—121° (Found : C, 57·9; H, 5·9; $C_{10}H_{12}O_3N_2$ requires C, 57·7; H, 5·8%), from dilute ethanol], potassium hydroxide (4 g.), and water (40 c.c.) maintained below −4°. When carbon dioxide evolution had ceased, the precipitate was collected and washed with ice-cold water and cold methanol, giving almost pure product (3·6 g.). *1 : 5-Di-o-methoxyphenyl-3-methylformazan* formed red plates (showing a blue reflex), m. p. 142—143° (Found : C, 64·3; H, 6·4. $C_{16}H_{18}O_2N_4$ requires C, 64·4; H, 6·1%), from dilute alcohol.

8-Methoxy-3-methylbenzo-1 : 2 : 4-triazine.—The formazan (1 g.), acetic acid (15 c.c.) and concentrated sulphuric acid (4 c.c.) at 0° gave an indigo solution which became brown after 1 min. at 95°. Heating was continued for 10 min., and there was then isolated in the usual way

(elution with benzene–ether) a mixture (0·35 g.) from which *8-methoxy-3-methylbenzo-1 : 2 : 4-triazine* (0·23 g.) [bright yellow plates, m. p. 124—125° (Found : C, 61·8; H, 5·1. $C_9H_9ON_3$ requires C, 61·7; H, 5·1%), from benzene–light petroleum] was sublimed (135—145°/1 mm.). The residue gave 1 : 6-dimethoxyphenazine (65 mg.), m. p. 253—254°, when crystallised from ethanol.

8-Methoxy-3-phenylbenzo-1 : 2 : 4-triazine.—*Benzaldehyde o-methoxyphenylhydrazone* (4·5 g.) [from benzaldehyde and *o*-methoxyphenylhydrazine in alcohol; needles, m. p. 88—90° (Found : C, 74·2; H, 6·6. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2%) from ethanol] in pyridine (36 c.c.) was stirred at 0° and treated with the diazonium solution from *o*-anisidine (2·5 g.), acetic acid (7 c.c.), concentrated sulphuric acid (2 c.c.), and sodium nitrite (1·4) g. in water (3 c.c.). After being stirred for 1 hr. at 0° and kept for 4 hr. at this temperature, the deep violet solution was diluted with water and extracted with chloroform. The washed and dried ($MgSO_4$) extract was concentrated, finally in a vacuum and the resulting permanganate-coloured oil was passed in benzene over alumina. The formazan (5·2 g.) was obtained as an oil which could not be crystallised.

The deep blue solution of this oil (4·8 g.) in acetic acid (70 c.c.) and concentrated sulphuric acid (20 c.c.) became brown after 2 min. at 95°; then the usual processing (elution with benzene) gave *8-methoxy-3-phenylbenzo-1 : 2 : 4-triazine* (1·3 g.) which formed yellow needles, m. p. 155—156° (Found : C, 70·2; H, 4·9; N, 17·9. $C_{14}H_{11}ON_3$ requires C, 70·8; H, 4·7; N, 17·7%), after sublimation (140°/1 mm.) and crystallisation from benzene–light petroleum.

The Action of Benzene and Aluminium Chloride on 8-Methoxybenzo-1 : 2 : 4-triazines.—(i) 8-Methoxybenzo-1 : 2 : 4-triazine (0·2 g.), benzene (10 c.c.), and anhydrous aluminium chloride (0·8 g.) were refluxed for 4 hr. Water was added, the aqueous layer was extracted with benzene, and the combined benzene solutions were extracted with dilute sodium hydroxide solution. The alkaline extract was washed with benzene, acidified with acetic acid, and extracted with benzene. Concentration of the benzene solution to a small volume gave a solid (110 mg.; m. p. 206—210°) which was sublimed (180—190°/1 mm.). The yellow sublimate formed from acetone glistening yellow platelets of a *product*, m. p. 238—239° (Found : C, 70·3; H, 4·0%; *M*, 209. $C_{13}H_9ON_3$ requires C, 69·9; H, 4·0%; *M*, 223. $C_7H_5ON_3,C_6H_6$ requires C, 69·3; H, 4·9%).

(ii) 8-Methoxy-3-methylbenzo-1 : 2 : 4-triazine (0·2 g.), treated with aluminium chloride and benzene, gave, in the way described above, a product which on sublimation (180—190°/1 mm.) provided a yellow solid (110 mg.). From acetone this *substance* formed shiny yellow plates, m. p. 177—178° (Found : C, 71·2; H, 4·9%; *M*, 211. $C_{14}H_{11}ON_3$ requires C, 70·9; H, 4·7%; *M*, 237. $C_8H_7ON_3,C_6H_6$ requires C, 70·3; H, 5·5%).

(iii) 8-Methoxy-3-phenylbenzo-1 : 2 : 4-triazine (0·2 g.) demethylated in the same way gave, after sublimation (180°/1 mm.) of the solid, a *product* (60 mg.) which formed woolly yellow needles, m. p. 213—214° (Found : C, 75·9; H, 4·3; N, 14·3. $C_{13}H_{13}ON_3$ requires C, 76·2; H, 4·4; N, 14·0. $C_{13}H_9ON_3,C_6H_6$ requires C, 75·7; H, 5·0; N, 13·95%), from benzene.

Attempted Cyclisation of 1 : 5-Di-p-methoxyphenylformazans.—1 : 5-Di-*p*-methoxyphenylformazan (2·75 g.; von Pechmann and Wedekind, *Ber.*, 1895, **28**, 1695), treated as described for the preparation of 8-methoxybenzo-1 : 2 : 4-triazine, gave, after chromatography, a pale yellow solid (20 mg.) (the colour and physical properties proved it not to be a triazine). Twice sublimed it had m. p. 109—113° (Found : C, 69·3; H, 5·7. Calc. for $C_{14}H_{12}O_2N_2$: C, 70·0; H, 5·0%). Tomlinson (*J.*, 1939, 161) gave m. p. 163° for 2 : 7-dimethoxyphenazine.

Pyruvic acid p-*methoxyphenylhydrazone* [needles, m. p. 142—143° (Found : C, 57·3; H, 5·8. $C_{10}H_{12}O_3N_2$ requires C, 57·7; H, 5·8%), from 30% ethanol], treated in the way described for the *o*-isomer, gave a solid red formazan which became tarry when collected. Application of cyclising conditions to this material produced no recognisable product.

1 : 5-Di-p-methoxyphenyl-3-phenylformazan.—The diazonium solution from *p*-anisidine (2·5 g.), acetic acid (7 c.c.), concentrated sulphuric acid (2 c.c.), and sodium nitrite (1·4 g.) in water (3 c.c.) was stirred into a solution of *benzaldehyde* p-*methoxyphenylhydrazone* (4·5 g.) [needles, m. p. 121—122° (Found : C, 74·2; H, 5·9. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2%), from alcohol] in pyridine (36 c.c.) at 0°. After being kept overnight at 0° the solution was diluted with water (200 c.c.), and the precipitate was washed with hot water and a little methyl alcohol. *1 : 5-Di-p-methoxyphenyl-3-phenylformazan* (4·3 g.) formed permanganate-coloured needles (olive-green reflex), m. p. 165—166° (Found : C, 70·0; H, 5·7. $C_{21}H_{20}O_2N_4$ requires C, 70·0; H, 5·6%), from ethanol.

6-Methoxy-3-phenylbenzo-1 : 2 : 4-triazine.—The formazan (1 g.) solution in acetic acid (15 c.c.) and concentrated sulphuric acid (4 c.c.) was heated at 95° until the colour changed from

deep blue to brown. The usual method (elution with benzene) gave *6-methoxy-3-phenylbenzo-1 : 2 : 4-triazine* (200 mg.) which formed shiny yellow plates, m. p. 197—198° (Found: C, 70·7; H, 4·8. $C_{14}H_{11}ON_3$ requires C, 70·9; H, 4%), from benzene.

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Pteridine Studies. Part VI. The Ultraviolet and Infrared Absorption Spectra of the Monosubstituted Pteridines.*

By S. F. MASON.

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The absorption spectra of a number of monosubstituted pteridines have been measured in the ultraviolet and the visible region, between 200 and 500 mμ, and in the infrared between 4000 and 400 cm.$^{-1}$. A band due to an $n \longrightarrow \pi$ transition has been identified in the ultraviolet spectrum of pteridine, the effect of substituents upon that band indicating that the electron involved in that transition is located upon the 8-nitrogen atom. Various infrared bands of pteridine have been assigned to particular vibrational modes by comparisons between the spectra of the substituted pteridines.

Ultraviolet Spectra.—Pteridine, 1 : 3 : 5 : 8-tetra-azanaphthalene, possesses a π-electron structure similar to that of naphthalene, though some localization of the π-electrons may be expected in the former owing to the high proportion of doubly-bound nitrogen. Accordingly, electronic transitions between the π-electron orbitals, and the ultraviolet absorption bands arising from such transitions, should display similarities due to the structural resemblance and differences due to the partial localization of π-electrons on the nitrogen atoms and the presence of non-bonding σ-electrons on those atoms. It is found that naphthalene, pteridine, and the monoazanaphthalenes (Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," Wiley and Sons, New York, London, 1951, Nos. 195, 270, and 271) give rise to similar spectra in the region 200—320 mμ (Fig. 1), consisting, in general, of three bands.

The band of the longest wavelength in the ultraviolet spectrum of naphthalene, that at 320 mμ, is of low intensity ($\varepsilon_{max.}$ 250), being due to a symmetry-forbidden transition, or to an allowed transition of accidentally zero moment † (Craig, *Rev. Pure Appl. Chem.*, 1953, **3**, 207), but the introduction of one or more nitrogen atoms effects a perturbation which gives rise to a corresponding band of much greater intensity. The maximum extinction coefficient of this band is 7080 for pteridine (see Table 1), whilst the value calculated by adding vectorially the spectroscopic moments of the four nitrogen atoms, on the assumption that the corresponding band in naphthalene is due to a transition of accidentaly zero moment (Platt, *J. Chem. Phys.*, 1951, **19**, 263) is 10,100. The second band in the naphthalene spectrum is not so greatly changed in intensity by the introduction of nitrogen atoms but it is shifted from 280 mμ in naphthalene to 235 mμ in pteridine. The third band in the naphthalene spectrum is of high intensity (ε 100,000), and in the azanaphthalenes is reduced in height (for pteridine, ε 11,000).

Pteridine differs from naphthalene in possessing some unshared electrons, namely, those on nitrogen. One of these non-bonding electrons can undergo a transition to an unoccupied π-orbital of the rings, giving rise to a low-intensity band (ε 84) at 380 mμ which has no counterpart in the spectrum of naphthalene. This band may be identified as due to an $n \longrightarrow \pi$ transition by its low intensity, which arises from the lack of overlap between a σ(*n*)- and a π-orbital; by the fact that it shifts towards shorter wavelengths on

* Part V, *J.*, 1954, 3832.

† Recent work (Sponer and Cooper, *J. Chem. Phys.*, 1955, **23**, 646) supports the latter view.

passage from a non-polar to a polar solvent, owing to interaction of the non-bondingelectrons with the polar solvent molecules; and by the disappearance of the band in acid solution, the non-bonding electrons of the nitrogen being more firmly held in pteridine cation (Kasha, *Discuss. Faraday Soc.*, 1950, **9**, 14; McConnell, *J. Chem. Phys.*, 1952, **20**, 700; Platt, *J. Opt. Soc. Amer.*, 1953, **43**, 252). In aqueous solution interaction between the solvent and the pteridine molecule stabilises the ground state but not the excited state, because the ground- and the excited-state charge distributions do not overlap strongly, and, owing

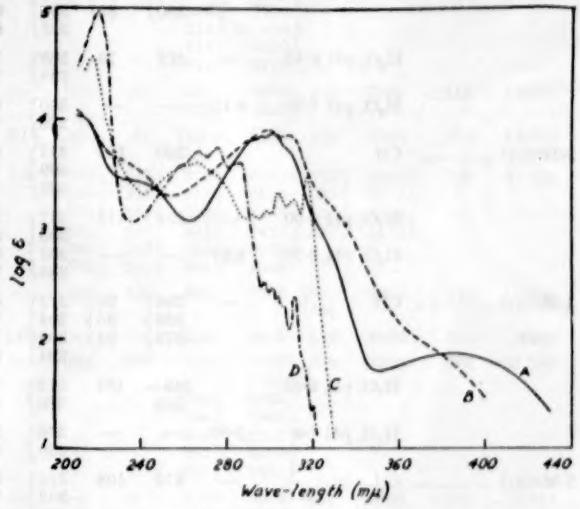


FIG. 1. *Ultraviolet absorption spectra of (A) pteridine in cyclohexane, (B) pteridine (neutral molecule), (C) isoquinoline in cyclohexane (Friedel and Orchin, op. cit., no. 271), and (D) naphthalene in 95% ethanol (ibid., no. 195).*

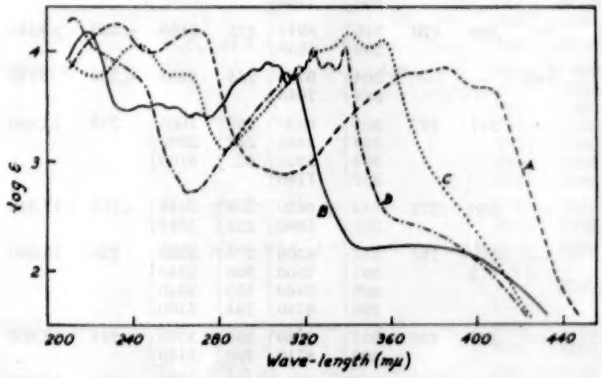


FIG. 2. *Ultraviolet absorption spectra of (A) 6-dimethylamino-, (B) 4-chloro-, (C) 7-methylthio-, and (D) 2-methoxy-pteridine, all in cyclohexane.*

to the operation of the Franck–Condon principle, the energy of the $n \longrightarrow \pi$ transition is increased, shifting the band derived from that transition to shorter wavelengths. The band origin of the $n \longrightarrow \pi$ transition in pteridine, and the methyl-, chloro-, and methoxy-pteridines, undergoes a shift of some 1400 cm.$^{-1}$ on passage from *cyclo*hexane to aqueous solution, indicating that the strength of the hydrogen bonding between water and the pteridines examined is some 4 kcal./mole.

Substituents in the pteridine nucleus leave unchanged, or exert a hypsochromic effect upon, the position of the $n \longrightarrow \pi$ band of the pteridine spectrum, whilst they exert a marked bathochromic effect upon the $\pi \longrightarrow \pi$ bands (Fig. 2 and Table 1), so that the $n \longrightarrow \pi$ band is obscured by the long-wave $\pi \longrightarrow \pi$ band in the spectra of the methylthio- and dimethylamino-pteridines. The energy levels of the π-orbitals, filled or unfilled, tend

TABLE 1. *The ultraviolet and visible absorption bands (mμ) of pteridine and its derivatives. Values in italics refer to shoulders or inflexions, and values in braces refer to fine-structure peaks in a given band. The bands are classified according to their intensities.*

Substituent	Solvent *	pK_a in H_2O	$\pi \rightarrow \pi$ band λ	$\pi \rightarrow \pi$ band ε	1st $\pi \rightarrow \pi$ band λ	1st $\pi \rightarrow \pi$ band ε	2nd $\pi \rightarrow \pi$ band λ	2nd $\pi \rightarrow \pi$ band ε	3rd and 4th $\pi \rightarrow \pi$ bands λ	3rd and 4th $\pi \rightarrow \pi$ bands ε
Parent)	CH	—	395 387 380	78 84 84	*308* 301 296 *292*	5570 7490 6950 6340	*235*	2910	210	11,000
	H_2O, pH 6·10	—	*375*	79	309 298	7180 7730	*230*	4480	<210	>12,500
	H_2O, pH 1·70	4·12	—	—	300 286	8320 7640	—	—	<210	>9660
2-Methyl	CH	—	380	125	317 309 305	5640 7420 7380	*235*	3050	212	10,620
	H_2O, pH 6·90	—	*370*	112	317 305	7940 8320	*230*	4790	<215	>10,440
	H_2O, pH 2·70	4·87	—	—	301 285	8040 7730	248	3890	<215	>4120
4-Methyl	CH	—	394 386 378	90 95 94	*311* 304 300 294	5050 7075 7050 6275	270 248 243	2075 2675 2670	216 —	14,200 —
	H_2O, pH 6·05	—	349— 353	163	312 300	7260 8420	*250*	2530	<220	>11,080
	H_2O, pH 1·0	2·90	—	—	306 280	9920 6120	—	—	<215	>14,120
7-Methyl	CH	—	375	108	*310* 302 298	6000 7720 7720	*239*	2750	212	9480
	H_2O, pH 6·90	—	*360*	170	310 298	8910 9550	*235*	3160	<220	>8240
	H_2O, pH 1·3	3·49	—	—	304 *285*	9770 7040	*255*	2350	<220	>3170
2-Chloro	CH	—	377	122	322 314 308 302	9250 8450 9220 7180	262 *243* *237*	1000 3900 5100	219	12,500
	H_2O, pH 7·0	—	*360*	277	319 307	8630 8990	258 *235*	2040 5010	<215	>17,040
4-Chloro	CH	—	371— 373	165	315 307 303 296	6200 7500 7860 6740	270 260 252 244	2760 3140 3340 3160	220	15,000
	H_2O, pH 7·0	—	*350*	236	315 303	7640 8710	255 250	3160 3160	218	13,800
6-Chloro	CH	—	*365*	131	323 315 309 303	7980 7540 8800 6960	*240*	4600	<220	>15,220
	H_2O, pH 7·0	—	—	—	323 315 309 303	7950 7540 8790 6910	*235*	5620	<215	>15,140
7-Chloro	CH	—	354— 355 344— 345	236 237	316 308 303 297	7860 8480 9080 7600	*240*	3000	217	10,000

TABLE 1. (*Continued.*)

Substituent	Solvent *	pK_a in H_2O	$n \rightarrow \pi$ band		1st $\pi \rightarrow \pi$ band		2nd $\pi \rightarrow \pi$ band		3rd and 4th $\pi \rightarrow \pi$ bands	
			λ	ε	λ	ε	λ	ε	λ	ε
	H_2O, pH 7·0	—	—	—	316 309 303	10,230 8870 9380	—	—	<215	>10,000
2-Methoxy	CH	—	*370*	250	339 331 324 318 311	10,640 7700 10,400 7080 6120	*238*	6720	213	19,700
	H_2O, pH 6·0	—	—	—	338 325	8080 8340	*240*	5500	<215	>17,620
	H_2O, pH 0	2·13	—	—	310—311	6380	*250*	5380	225	13,280
4-Methoxy	CH	—	389 381 374 367 360 353	143 212 261 287 286 268	319 313 307 301 295 291	6125 6025 8425 7425 6950 5675	273 263 255 *245*	2945 3025 2755 2165	226	21,700
	H_2O, pH 5·37	—	*350*	430	304	7730	257—260	2290	225	17,800
	H_2O, pH 1·0 *	1·04	—	—	302	9280	259	3400	218	8800
6-Methoxy	CH	—	*360*	292	331 323 316 309 303 297 291	9500 6780 9840 6500 6300 4320 3520	*240*	6300	216	20,700
	H_2O, pH 6·00	—	—	—	328 316 304	5620 6680 5700	*240*	5660	<215	>18,340
	H_2O, pH 1	3·60	—	—	288	12,380	—	—	<220	>14,720
7-Methoxy	CH	—	*340*	400	315 308 302 295 290 284 279	11,600 8700 11,680 8480 7800 5660 4500	254 *240*	1445 3940	214	18,300
	H_2O, pH 7·0	—	—	—	313 302	8910 9770	—	—	<215	>18,000
	H_2O, pH −0·8 *	1·64	—	—	298—300 275—277	6520 6240	—	—	220	21,360
2-Methylthio	CH	—	—	—	367 358	7720 7200	— —	— —	277 242	15,200 14,600
	H_2O, pH 5·50	—	—	—	360	7000	—	—	270 242	12,960 15,000
	H_2O, pH 0	2·2	—	—	*320*	6160	—	—	275 251	9840 20,800
4-Methylthio	CH	—	—	—	*364* *357* 348	7600 8040 9240	*295* 285	2580 2860	259 254 231	10,680 10,640 10,600
	H_2O, pH 4·90	—	—	—	353—354	8520	282—285	2760	254 238	8880 9000
	H_2O, pH 0	2·59	—	—	335	10,200	*290*	3840	232—233	9400
7-Methylthio	CH	—	—	—	356 341 331	12,200 14,360 10,240	263	6120	243	11,400

TABLE 1. (*Continued.*)

Substituent	Solvent [a]	pK_a in H_2O	$n \longrightarrow \pi$ band λ	$n \longrightarrow \pi$ band ε	1st $\pi \longrightarrow \pi$ band λ	1st $\pi \longrightarrow \pi$ band ε	2nd $\pi \longrightarrow \pi$ band λ	2nd $\pi \longrightarrow \pi$ band ε	3rd and 4th $\pi \longrightarrow \pi$ bands λ	3rd and 4th $\pi \longrightarrow \pi$ bands ε
	H_2O, pH 5·0	—	—	—	350	14,240	266	5560	240—241	9800
	H_2O, pH 0	2·50	—	—	343	10,840	278	4500	239	16,640
2-Dimethylamino	CH	—	—	—	434 441 390	4960 7280 6540	—	—	279 239	13,360 20,100
	H_2O, pH 7·1	—	—	—	410	6620	—	—	281—282	10,500
									236	23,200
	H_2O, pH 1·0	3·03	355—360	450	305	7940	—	—	237	14,500
4-Dimethylamino	CH	—	—	—	*378* 362	5880 8160	290—294	1650	260 256 252 235	13,320 12,920 12,880 14,200
	H_2O, pH 7·0	—	—	—	362	8500	—	—	241	14,400
	H_2O, pH 2·0	4·33	—	—	345	12,420	—	—	239	13,900
6-Dimethylamino	CH	—	—	—	403 384 *369*	4570 6920 6040	—	—	269 232	15,640 17,400
	H_2O, pH 7·0	—	—	—	399	5540	*310*	2600	278 231	14,600 16,520
	H_2O pH 2·0	4·31	—	—	*322*	9400	—	—	300—298 222	15,200 21,280
7-Dimethylamino	CH	—	—	—	379 362 *351*	5760 9360 8480	—	—	269 240	9240 17,960
	H_2O, pH 5·0	—	—	—	362—366 366	11,200	—	—	279—280 240	9480 15,640
	H_2O, pH 0·5 [c]	2·53	—	—	360—361	14,440	—	—	310—314 245	9160 8920
6 : 7-Dimethyl.....	CH	—	370—372	109	314 301	8000 9760	*240*	3480	<215	>14,520
	H_2O, pH 6·0	—	*350*	234	314 301	9700 10,460	*235*	3440	<215	>13,660
	H_2O, pH 1·0	2·93	—	—	307	11,320	260	3460	<220	>1960
2 : 6 : 7-Trimethyl	CH	—	368—373	113	321 312 307 301	9120 8840 10,160 8040	*240*	3960	<220	>13,860
	H_2O, pH 6·50	—	*350*	324	320 307	10,720 11,220	*235*	*5480*	<220	>14,720
	H_2O, pH 1·0	3·76	—	—	307	11,860	255—256	4480	<220	>3000
2 : 4 : 6 : 7-Tetrachloro	CH	—	*370*	405	343 337 327	11,520 9040 11,720	280	2160	238	19,780

[a] CH = *cyclo*hexane. [b] 5N-Sulphuric acid. [c] 4N-Sulphuric acid. [d] 0·33N-Hydrochloric acid.

to converge with increasing extranuclear conjugation, and, as expected, the bathochromic effect of substituents in the pteridine nucleus on the $\pi \longrightarrow \pi$ bands increases with the mesomeric effect of those substituents (Table 1), but the $\sigma(n)$-orbitals are localized and their binding energies are less affected by extranuclear conjugation. The hypsochromic effect of substituents on the $n \longrightarrow \pi$ band, which increases in the order Me < Cl < OMe, indicates that the unshared electrons of the nuclear nitrogen atoms are more firmly held in the

substituted pteridines than in pteridine itself, because the π-orbital to which such an electron is excited is of lower energy in a substituted pteridine than in the parent molecule. In conformity with this indication it is found that the basic ionization constants of the known methyl- and methoxy-pteridines are lower than that of pteridine itself, except for 2-methylpteridine (Table 1). However, the base-weakening effect of a given substituent in the pteridine nucleus does not closely parallel its hypsochromic effect on the $n \longrightarrow \pi$ band of the pteridine spectrum, for the nitrogen atom from which the $n \longrightarrow \pi$ transition originates is not necessarily the basic centre of the pteridine molecule.

The most likely location of the non-bonding electron responsible for the $n \longrightarrow \pi$ band of the pteridine spectrum is the 8-nitrogen atom of the nucleus, because $n \longrightarrow \pi$ transitions are particularly sensitive to inductive effects (Goodman and Shull, *J. Chem. Phys.*, 1954, **22**, 1138), and substituents placed in the 7-position of pteridine exert a larger hypsochromic effect on the $n \longrightarrow \pi$ band of the pteridine spectrum, and enhance its intensity to a greater degree than when placed elsewhere (Table 1). However, the other nuclear nitrogen atoms contribute to the $n \longrightarrow \pi$ transition by interaction with the 8-nitrogen atom, since no $n \longrightarrow \pi$ band is observed in the spectrum of quinoline or *iso*quinoline. Interaction is more effective between 1 : 4- than between 1 : 3-aza-atoms, the $n \longrightarrow \pi$ band of pyrazine being of lower energy and more intense than that of pyrimidine (Halverson and Hirt, *J. Chem. Phys.*, 1951, **19**, 711); and of the two nitrogen atoms in the pyrazine ring of the pteridine nucleus, only that in the 8-position can compensate to some degree for the electron depletion caused by the inductive effect of a vicinal substituent by conjugation with the nitrogen atoms of the pyrimidine ring.

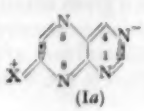
The effects of substituents on the π-electron spectra of pteridine and naphthalene show some similarities in regard to the bathochromic shifts induced by such substituents but not in respect of the intensity changes consequent upon substitution. A 2-substituent in naphthalene exerts a greater bathochromic effect upon the 320-mμ band of the naphthalene spectrum than a 1-substituent, whilst the reverse is true for the 280-mμ band (Friedel and Orchin, *op. cit.*, Nos. 196, 197, 236, 237, 250, 251, 264, and 265). In the spectrum of quinoline a substituent gives rise to similar relative bathochromic shifts when placed α or β to the bridge carbon atoms (Friedel and Orchin, *op. cit.*, Nos. 272—275); but for pteridine the parallel is not quite so close, for its 300-mμ band is moved towards longer wavelengths to approximately the same degree (Table 1) when a given substituent is placed in either the 4- or the 7-position, these being an α and a β position respectively. However, a substituent exerts the greatest bathochromic shift of the 235-mμ band of pteridine when it is in the 4-position, and a larger shift of the 300-mμ band when in the 2- or the 6-position than when in the 4-position.

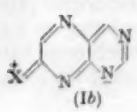
In general, substituents in any given position of the pteridine nucleus exert a bathochromic effect on the 300-mμ band which increases in the order Me < Cl < OMe < SMe < NMe_2. These substituents follow the same order in regard to their bathochromic effect on the 260-mμ band of the benzene spectrum (Bowden and Braude, *J.*, 1952, 1068), and, so far as information is available, on the 320-mμ band of the naphthalene spectrum (Friedel and Orchin, *op. cit.*; Ferguson, *J.*, 1954, 304), a band which has been related by a spectroscopic sequence to the 260-mμ band of the benzene spectrum (Platt, *J. Chem. Phys.*, 1951, **19**, 101) and is taken in the present work as corresponding to the 300-mμ band of the pteridine spectrum. However, a given substituent produces a larger bathochromic shift of the pteridine spectrum than of the benzene and naphthalene spectra, the shift being very much larger when the substituent is introduced into the 2- or the 6-position.

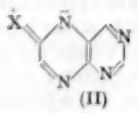
Turning now from the consideration of wavelength shifts consequent upon substitution to changes of intensity, which are susceptible to more precise theoretical treatment in the case of cata-condensed hydrocarbons and their derivatives, it is found that there are considerable divergences between the effects of substituents on the spectra of naphthalene and pteridine. The intensity changes of the 260-mμ band of benzene and the 320-mμ band of naphthalene produced by a substituent may be accounted for quantitatively according to the theory of Sklar (*J. Chem. Phys.*, 1942, **10**, 135) and Forster (*Z. Naturforsch.*, 1947, **2**, a, 149), as developed by Platt (*J. Chem. Phys.*, 1951, **19**, 263) on the assumption

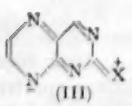
that these bands are due to an allowed transition of accidentally zero moment. Applied to pteridine, this theory indicates that a given substituent should increase the intensity in the 300-mμ band of the pteridine spectrum, as a function of its position in the nucleus, in the following order: $4 < 0 < 7 < 2 = 6$. It is found, however, that a substituent in the pteridine nucleus always enhances the intensity of the 300-mμ band most when in the 7-position (average $\Delta\varepsilon$ 2280, for the substituents studied), and least, in general, when placed in the 6-position (average $\Delta\varepsilon$ 117), the effects of 2- and 4-substitution being about equal (average $\Delta\varepsilon$ 456 and 540 respectively).

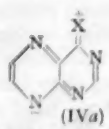
The intensity changes in the 300-mμ band of the pteridine spectrum consequent upon monosubstitution may be explained more readily in terms of a transition to an excited state with a transannular polarity (Lewis and Calvin, *Chem. Rev.*, 1939, **25**, 273), than of one to an excited state with alternant polarities round the perimeter of the nulceus (Platt, *loc. cit.*). The localization of π-electrons on the nitrogen atoms of the pteridine nucleus, which has been calculated according to both the molecular-orbital and the valence-bond method (Albert, *Quart. Rev.*, 1952, **6**, 197), confers a dipole moment on the molecule, owing to its asymmetry, so that transannular polarized structures may be expected to contribute even to the ground state of the molecule. A 7-substituted pteridine can form two excited structures with transannular polarity (I*a* and I*b*), the separation of charge being particularly large in (I*a*), whereas a 6-substituted pteridine can form the polarized structure (II) only, if a negative charge is located on a nuclear nitrogen atom and a positive charge on the substituent. 2- and 4-Substituted pteridines can form the polarized transannular structures (III) and (IV*a*) respectively, but in neither case is the separation of charge as large as in (I*a*). If the polarized structures (I—IV) make an important contribution to the excited states of the monosubstituted pteridines in the 300-mμ transition, then the intensity of that transition may be expected to be the highest in the 7-substituted pteridines and lowest in the 6-substituted, as the separation of charge during the transition is the greatest in the former and the smallest in the latter. Further, such a large separation of charge in the 7-substituted pteridines during the 300-mμ transition would require a larger amount of energy than is necessary for the other monosubstituted pteridines, thus accounting for the fact that a given 7-substituent in pteridine exerts a smaller bathochromic effect on the 300-mμ band than when it is placed elsewhere β to the bridge carbon atoms, namely, in the 2- or the 6-position.

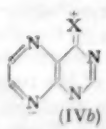

(I*a*)


(I*b*)


(II)


(III)


(IV*a*)


(IV*b*)

A substituent exerts its greatest bathochromic effect on the low-intensity 235-mμ band of the pteridine spectrum when in the 4-position, and the band becomes well defined in this case, showing fine structure (Fig. 2), whilst it remains a shoulder on the side of the higher-intensity band at shorter wavelengths, or is submerged under that band, when the substituent is elsewhere. The 4-substituted pteridines may form excited structures (IV*a* and IV*b*) with a more extended conjugation along the short axis of the molecule than is possible with other monosubstituted pteridines. Accordingly, it is likely that the 235-mμ transition in the pteridine spectrum is polarized along the short axis of the molecule whilst the 300-mμ transition is polarized along the long axis.

Pteridine and its monosubstituted derivatives exhibit, in *cyclo*hexane solution, fine structure in the long-wave band of the π-electron spectrum, and in some cases the $n \longrightarrow \pi$ and the second and third $\pi \longrightarrow \pi$ bands as well. The character of the fine structure in the long-wave band varies with the nature of the substituent rather than its position, whilst

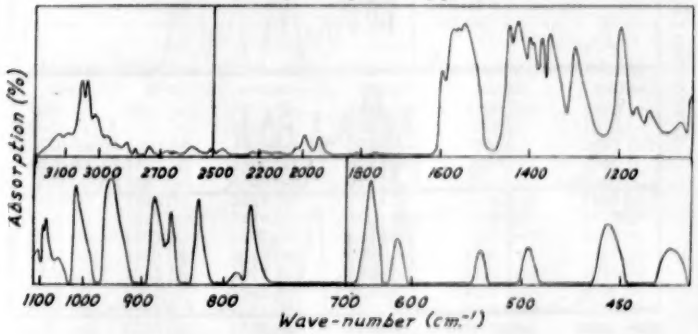
fine structure in the other bands depends on the position of the substituent, for it is confined almost exclusively to the spectra of the 4-substituted pteridines. The methoxypteridines, for example, show an alternation in the intensity and spacing of the fine-structure peaks of the long-wave band in their π-electron spectra (Fig. 2, Table 1), suggesting that principally two vibrations are active in the transition. Some alternation in the intensities of the fine-structure peaks of this band is observed in the spectra of the chloropteridines; and in those of the methylthio- and the dimethylamino-pteridines, where the fine structure is not sharp, the spacings between the peaks are twice as large as those found in the first $\pi \longrightarrow \pi$ band of the other monosubstituted pteridines, spacings which may arise from the submergence of alternant low-intensity peaks. The fine-structure spacings in this band lie in the range of 400—850 cm.$^{-1}$ for pteridine and its methyl-, chloro-, and methoxy-derivatives, a range which covers mainly nuclear bending and distortion vibrations. Spacings of the same order are observed in the third $\pi \longrightarrow \pi$ band of 4-methylthio- and 4-dimethylamino-pteridine (760 and 610 cm.$^{-1}$ respectively), whilst spacings twice as large are found

TABLE 2. *Infrared absorption bands (cm.$^{-1}$) of pteridine between 4000 and 400 cm.$^{-1}$.*

s = strong, m = medium, w = weak absorption.

3117 w,	3090 w,	3055 m,	3035 m,	3013 w,	2951 w,	2917 w,	2854 w,	2806 w,	2784 w,	2670 w,
2636 w,	2568 w,	2508 w,	2445 w,	2240 w,	2170 w,	2115 w,	2025 w,	2000 w,	1940 w,	1820 w,
1763 w,	1603 m,	1580 s,	1573 s,	1558 s,	1461 s,	1435 s,	1400 s,	1391 s,	1368 s,	1348 s,
1286 s,	1197 s,	1176 w,	1158 w,	1109 w,	1092 m,	1085 m,	1056 w,	1015 s,	933 s,	882 s,
860 s,	822 s,	795 w,	777 s,	653 s,	616 m,	533 m,	497 m,	455 m,	434 m	

FIG. 3. *Infrared spectrum of pteridine.*

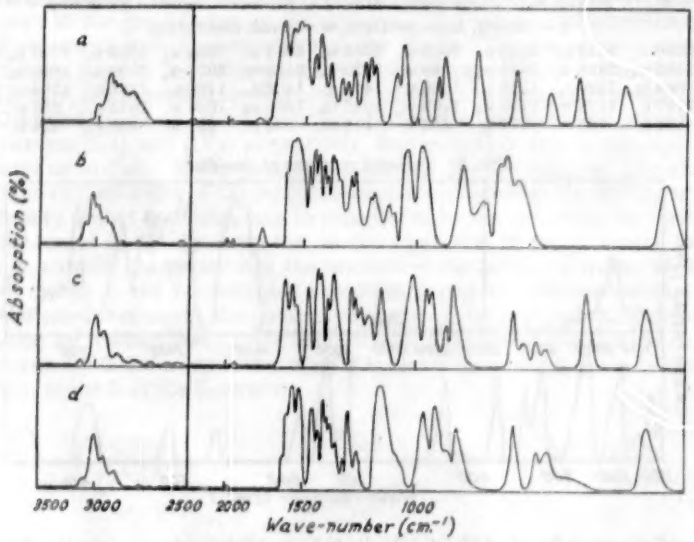


in the second $\pi \longrightarrow \pi$ band of the 4-substituted pteridines, where again the fine structure is not sharp and the apparently large spacings may be due to the submergence of low-intensity peaks. Fine structure in the $n \longrightarrow \pi$ band, which occurs in the spectra of pteridine and its 4-methyl- and 4-methoxy-derivatives, is not so well defined as that of the first $\pi \longrightarrow \pi$ band, but the intensities of the individual peaks in the $n \longrightarrow \pi$ band are more regular and the spacings more uniform (500—550 cm.$^{-1}$), suggesting that a single vibration may be active in the transition, as would be expected in view of the localized character of the non-bonding electron orbital (Kasha, *loc. cit.*).

Infrared Spectra.—Pteridine possesses thirty-six possible modes of vibration, and, the molecule being of low symmetry, most of these vibrations should be active in the infrared. The infrared absorption spectrum of pteridine exhibits some fifty bands between 3500 and 400 cm.$^{-1}$ (Fig. 3, Table 2), the twenty or so weak bands above 1600 cm.$^{-1}$ probably including many overtone or combination absorptions. Between 400 and 700 cm.$^{-1}$ pteridine gives rise to six absorption bands, which, by analogy with the assigned bands in the same region of the naphthalene spectrum (Lippincott and O'Reilly, *J. Chem. Phys.*, 1955, **23**, 238), are likely to be due to skeletal vibrations. Of the seven bands in the pteridine spectrum between 700 and 1050 cm.$^{-1}$, that at 777 cm.$^{-1}$ is connected with the presence of a 4-C–H bond, and may be due to the out-of-plane bending vibration of that

bond, since a corresponding band is found in the spectra of all of the 2-, 6-, and 7-monosubstituted pteridines examined, but not in the spectra of any 4-monosubstituted pteridine (Fig. 4, Table 3). Similarly the 860- and 882-cm.$^{-1}$ bands in the spectrum of pteridine may arise from the 6- and 7-C–H bending vibrations, as corresponding bands are observed in the spectra of the 2- and 4-monosubstituted pteridines, but not in the spectra of the 6- or 7-substituted derivatives, except for 6- and 7-dimethylaminopteridine, which absorb at 880 and 888 cm.$^{-1}$ respectively. 6- and 7-Aminopteridine * do not absorb in this region, so the 880- and 888-cm.$^{-1}$ bands in the dimethylamino-derivatives are probably due to a vibration of the substituent group. However, the 860-cm.$^{-1}$ band is absent from the spectra of most of the 2-substituted pteridines also, indicating that the 2-H–C bond is probably involved in the vibration giving rise to this band. It is unsual that the two adjacent C–H bonds in the 6- and the 7-position of pteridine should undergo out-of-plane deformation vibrations which absorb at a higher frequency than the corresponding vibration

FIG. 4. *Infrared spectrum of* (*a*) *2-dimethylamino-*, (*b*) *4-chloro-*, (*c*) *6-methoxy-*, *and* (*d*) *7-methylthiopteridine.*



of the single C–H bond in the 4-position, since the normal ranges of 860—900 cm.$^{-1}$ for one free hydrogen atom, and 800—860 cm.$^{-1}$ for two adjacent hydrogen atoms attached to an aromatic nucleus, seem to obtain even in heterocyclic systems (Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 235). Indeed the value of 777 cm.$^{-1}$ for the proposed 4-C–H distortion vibration is low even for a single hydrogen atom attached to an ethylenic system, a group which absorbs in the range 790—840 cm.$^{-1}$ (Bellamy, *op. cit.*, p. 31). There is some doubt whether the 777-, 860-, and 882-cm.$^{-1}$ bands of the pteridine spectrum are due to C–H deformation vibrations since comparable bands at 784, 868, and 874 cm.$^{-1}$ occur in the spectrum of tetrachloropteridine, though it is possible that the latter set is due to C–Cl stretching vibrations.

In the same region, pteridine also shows bands at 822, 933, and 1015 cm.$^{-1}$, probably due to skeletal vibrations as corresponding bands are found in the spectra of all of the substituted pteridines examined. The 822-cm.$^{-1}$ band is particularly well marked in intensity and position, and displays an interesting substitution effect. The corresponding band in the pteridines substituted β to the bridge carbon atoms lies in the range 817—

* It is hoped to discuss the ultraviolet and infrared absorption spectra of the pteridines substituted with a potentially tautomeric group in a later paper.

TABLE 3. *Infrared absorption bands (cm.$^{-1}$) of some substituted pteridines between 2000 and 700 cm.$^{-1}$.*

2-Methyl	4-Methyl	7-Methyl	2-Chloro	4-Chloro	2-Methoxy	4-Methoxy	6-Methoxy	7-Methoxy
2000 (w)	2000 (w)	1990 (w)	2000 (w)	2000 (w)	2050 (w)	1985 (w)	1905 (w)	1955 (w)
1915 (w)	1940 (w)	1945 (w)	1570 (s)	1940 (w)	1598 (s)	1578 (s)	1591 (s)	1930 (w)
1590 (s)	1567 (s)	1585 (m)	1564 (s)	1710 (w)	1560 (s)	1570 (s)	1560 (s)	1860 (w)
1570 (s)	1558 (s)	1567 (s)	1544 (s)	1570 (m)	1543 (s)	1555 (s)	1546 (m)	—
1552 (s)	1546 (s)	1556 (s)	1445 (m)	1558 (s)	1494 (s)	1497 (s)	1472 (s)	1591 (m)
1442 (s)	1473 (m)	1526 (w)	1430 (s)	1540 (s)	1450 (s)	1471 (m)	1394 (s)	1570 (s)
1389 (m)	1458 (s)	1436 (s)	1424 (s)	1458 (m)	1393 (s)	1444 (w)	1374 (s)	1560 (s)
1375 (m)	1436 (m)	1407 (w)	1363 (m)	1423 (s)	1347 (w)	1420 (m)	1333 (m)	1546 (s)
1338 (m)	1399 (w)	1389 (m)	1345 (m)	1393 (s)	1326 (w)	1406 (s)	1298 (s)	1487 (m)
1312 (m)	1374 (m)	1361 (s)	1328 (m)	1359 (m)	1276 (m)	1372 (m)	1212 (s)	1468 (s)
1254 (s)	1357 (w)	1342 (m)	1304 (w)	1336 (w)	1240 (w)	1349 (s)	1195 (m)	1394 (s)
1192 (w)	1330 (w)	1295 (w)	1289 (m)	1310 (s)	1203 (m)	1305 (w)	1172 (m)	1372 (s)
1153 (m)	1304 (w)	1270 (s)	1261 (w)	1295 (s)	1186 (w)	1279 (w)	1141 (m)	1321 (m)
1102 (w)	1260 (s)	1221 (w)	1244 (w)	1218 (m)	1168 (m)	1222(w)	1100 (s)	1307 (s)
1079 (w)	1215 (w)	1201 (s)	1210 (s)	1200 (m)	1131 (w)	1184 (w)	1010 (s)	1281 (m)
1038 (s)	1117 (w)	1162 (s)	1172 (w)	1136 (w)	1080 (w)	1172 (m)	975 (s)	1207 (s)
1024 (m)	1080 (s)	1098 (m)	1160 (w)	1126 (w)	1043 (s)	1118 (s)	964 (s)	1191 (m)
1006 (m)	1029 (w)	1089 (m)	1129 (s)	1077 (w)	1018 (s)	1024 (s)	932 (w)	1115 (w)
966 (m)	1015 (s)	1036 (m)	1091 (w)	1062 (w)	983 (w)	986 (w)	920 (s)	1104 (w)
951 (s)	997 (w)	1006 (w)	1016 (s)	1026 (s)	963 (w)	970 (s)	824 (m)	1018 (s)
910 (w)	972 (w)	956 (s)	988 (w)	991 (s)	948 (s)	891 (s)	811 (w)	971 (m)
885 (s)	958 (m)	915 (s)	971 (w)	903 (s)	889 (m)	882 (m)	795 (w)	963 (m)
829 (s)	888 (s)	829 (s)	951 (s)	870 (w)	880 (w)	860 (m)	784 (w)	935 (s)
788 (s)	860 (s)	800 (m)	890 (s)	862 (w)	866 (m)	855 (s)	741 (s)	823 (m)
759 (w)	835 (s)	790 (m)	828 (m)	844 (s)	829 (s)	839 (s)	688 (s)	810 (w)
741 (s)	705 (w)	702 (w)	785 (s)	835 (s)	793 (m)	742 (s)	—	790 (m)
689 (s)	—	678 (s)	716 (m)	820 (m)	758 (s)	715 (s)	—	720 (s)
—	—	—	—	678 (m)	746 (w)	—	—	—

2-Methyl-thio	4-Methyl-thio	7-Methyl-thio	2-Dimethyl-amino	4-Dimethyl-amino	6-Dimethyl-amino	7-Dimethyl-amino	2 : 4 : 6 : 7-Tetra-chloro
1580 (s)	1980 (w)	1985 (w)	1970 (w)	1945 (w)	1930 (w)	1985 (w)	2000 (w)
1561 (s)	1945 (w)	1586 (w)	1740 (w)	1580 (s)	1596 (s)	1915 (w)	1697 (m)
1537 (s)	1570 (m)	1573 (m)	1610 (s)	1558 (s)	1560 (s)	1601 (m)	1567 (s)
1434 (s)	1555 (s)	1555 (s)	1570 (s)	1540 (s)	1537 (s)	1560 (s)	1546 (s)
1367 (m)	1537 (s)	1525 (s)	1540 (s)	1522 (s)	1506 (m)	1525 (s)	1516 (s)
1349 (w)	1457 (s)	1434 (s)	1528 (s)	1493 (s)	1435 (m)	1435 (s)	1397 (s)
1290 (m)	1428 (s)	1387 (m)	1444 (m)	1420 (m)	1393 (s)	1417 (s)	1379 (s)
1281 (m)	1391 (s)	1353 (s)	1425 (s)	1408 (s)	1340 (w)	1398 (s)	1281 (s)
1222 (m)	1321 (m)	1330 (s)	1337 (m)	1387 (m)	1300 (w)	1382 (s)	1270 (s)
1216 (s)	1304 (s)	1312 (m)	1275 (w)	1330 (m)	1256 (m)	1370 (s)	1237 (s)
1161 (w)	1283 (s)	1305 (m)	1246 (m)	1313 (s)	1221 (w)	1339 (s)	1200 (s)
1139 (w)	1220 (m)	1283 (w)	1217 (m)	1275 (s)	1164 (m)	1280 (w)	1190 (m)
1129 (s)	1194 (w)	1236 (w)	1167 (m)	1254 (m)	1103 (m)	1250 (m)	1141 (s)
1024 (s)	1158 (w)	1227 (s)	1150 (m)	1208 (m)	1062 (w)	1230 (w)	1073 (w)
1017 (s)	1127 (w)	1184 (w)	1132 (m)	1150 (w)	1012 (s)	1172 (m)	1035 (s)
976 (m)	1053 (w)	1097 (s)	1057 (m)	1098 (s)	940 (s)	1123 (w)	980 (w)
958 (w)	1030 (s)	1024 (w)	1042 (s)	1064 (w)	918 (w)	1100 (m)	874 (s)
943 (s)	997 (s)	978 (s)	990 (m)	1032 (m)	880 (m)	1065 (w)	868 (m)
900 (w)	980 (m)	953 (s)	955 (m)	984 (w)	817 (m)	1002 (m)	813 (m)
877 (m)	891 (m)	928 (w)	943 (s)	950 (w)	787 (m)	937 (s)	784 (m)
824 (s)	875 (w)	910 (m)	883 (s)	878 (m)	697 (m)	917 (w)	725 (m)
780 (s)	843 (s)	821 (m)	822 (m)	860 (s)	683 (s)	888 (s)	—
712 (m)	834 (s)	791 (m)	791 (m)	851 (m)	—	818 (s)	—
—	—	779 (m)	750 (m)	834 (s)	—	783 (m)	—
—	—	758 (w)	710 (m)	715 (m)	—	713 (w)	—
—	—	686 (s)	—	—	—	—	—

829 cm.$^{-1}$ and, in the pteridines substituted α to those atoms, between 834 and 839 cm.$^{-1}$. It seems, therefore, that the 822-cm.$^{-1}$ vibration of pteridine involves mainly the movement of the nuclear atoms of the molecule, the movement perhaps being that of the atoms α to the bridge carbon atoms of the pteridine rings, because substituents attached to such an α atom displace the band to a greater degree than the same substituents attached to a β atom. The 933- and 1015-cm.$^{-1}$ bands of the pteridine spectrum vary more widely in position than the 822-cm.$^{-1}$ band in the spectra of the substituted pteridines, probably owing to greater involvement of the extranuclear atoms in the vibrations giving rise to these bands.

Between 1050 and 1180 cm.$^{-1}$ in the spectrum of pteridine occur six bands of moderate or weak intensity, which are likely to be due to C–H bending vibrations, since comparable bands are not observed in the spectrum of tetrachloropteridine and such vibrations in other aromatic systems absorb in the same region. The spectra of the monosubstituted pteridines exhibit similar bands in the same region, but, unlike the case of the substituted benzenes, the locations of these bands do not seem to be characteristic of the particular positions of substitution.

From 1200 to 1500 cm.$^{-1}$ the spectra of pteridine and its derivatives are complex, and no satisfactory correlations between the spectra can be made. In the ring-stretching vibration region, three bands are observed in the spectra of all of the pteridine derivatives examined in the ranges 1610—1565, 1570—1545, and 1560—1515 cm.$^{-1}$ respectively. Substituents containing comparatively heavy atoms linked immediately to the nucleus, namely, the chloro- and methylthio-groups, displace the 1610—1565-cm.$^{-1}$ band towards the lower extremity of its range, just as they lower the frequency of the 1600-cm.$^{-1}$ ring-stretching vibration in benzene (Bellamy, *op. cit.*, p. 60). Moreover, the frequency of the 1610—1565-cm.$^{-1}$ band for a given substituent is highest when it is in the 2-position, though not much higher than when in the 6- or the 7-position, and lowest when in the 4-position. It seems likely, therefore, that the 1610—1565-cm.$^{-1}$ band in the spectra of the pteridines is due to a ring-stretching vibration which involves the movement of atoms immediately attached to the nucleus, particularly those substituted in the 4-position. The position of the 1610—1565-cm.$^{-1}$ band in the spectra of the monosubstituted pteridines is also affected by the mesomeric capacity of the substituent. For substituents in which the masses of the atoms directly attached to the nucleus are of the same order, the frequency of the band, for a given position of substitution, increases with the mesomeric effect of the substituent in the sequence: Me < OMe < NMe_2 and Cl ≪ SMe. The mesomeric effect of these substituents enhances the π-electron density of the pteridine nucleus, and so strengthens the nuclear bonds, producing ring-stretching vibrations of higher frequencies.

Between 1650 and 2800 cm.$^{-1}$ the spectra of pteridine and its derivatives show a number of weak bands which are probably due to overtone and combination absorptions. The absorption pattern between 1650 and 2000 cm.$^{-1}$ in the substituted pteridines, unlike that in the benzene series, does not seem to be characteristic of the substitution type. Finally, in the C–H stretching vibration region, pteridine gives rise to two moderately intense bands of 3035 and 3055 cm.$^{-1}$ with weaker bands on either side, whilst the monosubstituted pteridines show one moderately intense band, usually near 3050 cm.$^{-1}$.

Experimental

Materials.—The sources of the mono-, di-, and tri-substituted pteridines were as given by Albert, Brown, and Cheeseman (*J.*, 1951, 474; 1952, 1620, 4219) and Albert, Brown, and Wood (*J.*, 1954, 3832). 2 : 4 : 6 : 7-Tetrachloropteridine was prepared by the method of Shöpf, Reichert, and Riefstahl (*Annalen*, 1941, **548**, 82).

Ultraviolet Spectra.—These were measured with a Hilger Uvispek H700/301 Quartz Spectrophotometer, using *cyclo*hexane solutions and buffer solutions with the pH values recorded in Table 1. The buffer solutions were 0·01M-glycine (for pH 1·5—3·5), 0·01M-acetate (for pH 3·8—5·7), 0·01M-phosphate (for pH 6·0—7·9), together with N- (pH 0) and 0·1N-hydrochloric acid (pH 1·0).

Infrared Spectra.—These were measured with a Perkin-Elmer model 12C spectrometer, with prisms of lithium fluoride, sodium chloride, and potassium bromide. The compounds were examined as solids included in pressed potassium bromide discs.

The author thanks Mr. E. P. Serjeant and Mr. A. Bennett for help with the ultraviolet spectroscopy.

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p-*Hydroxybenzoate Groups in the Lignin of Aspen* (Populus tremula).

By D. C. C. Smith.

[Reprint Order No. 6160.]

The lignin of aspen wood contains *p*-hydroxybenzoate groups. They occur singly, involving aliphatic hydroxyl groups of the "native lignin," and account for about 10% of its weight.

"Native lignins," the soluble analogues of lignins which are the aromatic substances of high molecular weight associated with woodiness in plants (Percival, *Ann. Reports*, **1942**, **39**, 142; Brauns, "The Chemistry of Lignin," Academic Press Inc., New York, 1952), have an ultraviolet absorption spectrum in neutral solvents (Brauns, *J. Org. Chem.*, **1945**, **10**, 211; Kudzin and Nord, *J. Amer. Chem. Soc.*, 1951, **73**, 690; Enslin, *J. Sci. Food Agric.*, 1952, **4**, 318; Farmer, *Research*, **1953**, **6**, 47) with a characteristic band at 275—285 mμ indicative of an *O*-substituted benzene ring (Jones, *Techn. Assoc. Papers, TAPPI*, **1949**, **32**, 311). This band shifts to longer wavelengths and greater intensity in alkaline media, owing to ionisation of phenolic groups (Aulin-Erdtman, *Svensk Papperstidning*, **1952**, **44**, 745; Goldschmid, *J. Amer. Chem. Soc.*, **1953**, **75**, 3780).

The absorption spectrum of native lignin from aspen differs from those described above by having no defined maximum in neutral solvents (Brauns, Buchanan, and Leaf, *ibid.*, 1949, **71**, 1297). In the present work this lignin was found to show an abnormally large band at 295 mμ in alkaline solution. In 0·01N-sodium hydroxide this remained unchanged, but in N-sodium hydroxide it was slowly replaced by a broader band at 280 mμ. After treatment with N-alkali the lignin was separated into three fractions: A, insoluble in water at pH 4; B, soluble in water at pH 4 but not extracted by ether; and C, both soluble in water at pH 4 and extracted by ether. In alkali, fraction C had a broad absorption band at 280 mμ, thus resembling *p*-hydroxybenzoic acid, whereas fractions A and B showed absorption spectra of the type hitherto considered typical of lignins (Jones, *loc. cit.*). Spectra of the fractions are given in Fig. 1.

Examination of fraction C on paper chromatograms, using as solvents benzene–acetic acid–water and butanol–water (buffered paper), revealed that it was a complex mixture. *p*-Hydroxybenzoic acid, vanillic acid, syringic acid, and ferulic acid (4-hydroxy-3-methoxycinnamic acid) were identified on the chromatograms by comparison with known specimens. The related acids, *p*-coumaric acid and sinapic acid (4-hydroxy-3 : 5-dimethoxycinnamic acid), were not detected. Recrystallisation of fraction C yielded *p*-hydroxybenzoic acid (6·9% yield from the native lignin; the extinction of fraction C at 280 mμ corresponds to 12·2% of *p*-hydroxybenzoic acid, but other acids detected also absorb at this wavelength).

The absorption spectrum and the absence of material soluble in ether both indicate that free *p*-hydroxybenzoic acid is not present in native lignin, and the ease with which *p*-hydroxybenzoic acid is liberated suggests that it is present in an ester linkage. This could be formed either as lignin-O·CO·C_6H_4·OH (I), or as lignin-CO·O·C_6H_4·CO_2H (II), or as a depside-like polymer, produced by self-esterification of *p*-hydroxybenzoic acid, combined or physically associated with the lignin. To test these possibilities, the absorption spectra and rates of alkaline hydrolysis of three esters of *p*-hydroxybenzoic acid which simulate these types of linkage were compared with that of native lignin, as shown in the Table.

	Absorption max. in aq. NaOH (mμ)	Half-time of hydrolysis at 18° (min.)	(concn. of NaOH)
p-Acetoxybenzoic acid	228 *	1·2	0·01N
4-*p*-Hydroxybenzoyloxybenzoic acid	304	4·5	N
Methyl *p*-hydroxybenzoate	295	17	N
Aspen native lignin	295	39	N

* Measured in 1% sodium hydrogen carbonate.

The figures for *p*-acetoxybenzoic acid clearly rule out consideration of a linkage of type II, whereas the absorption maxima of native lignin and of methyl *p*-hydroxybenzoate are

at identical wavelengths. The absorption of the terminal phenolic nucleus of 4-*p*-hydroxybenzoyloxybenzoic acid shows a bathochromic shift of 9 mμ due to the adjacent aromatic

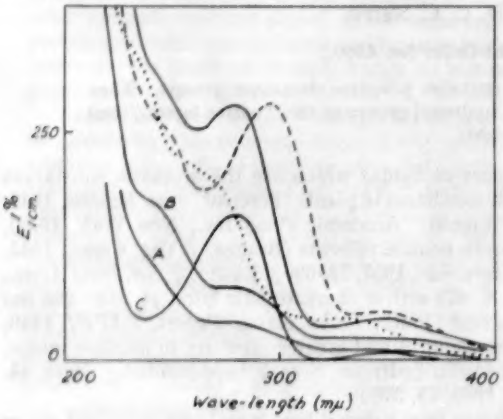


FIG. 1. *Absorption spectra of aspen native lignin.*

. . . . In MeOH.

– – – – In aqueous 0·01N-sodium hydroxide before hydrolysis.

——— In aqueous N-sodium hydroxide after hydrolysis.

A, B, and C are the fractions described in the text.

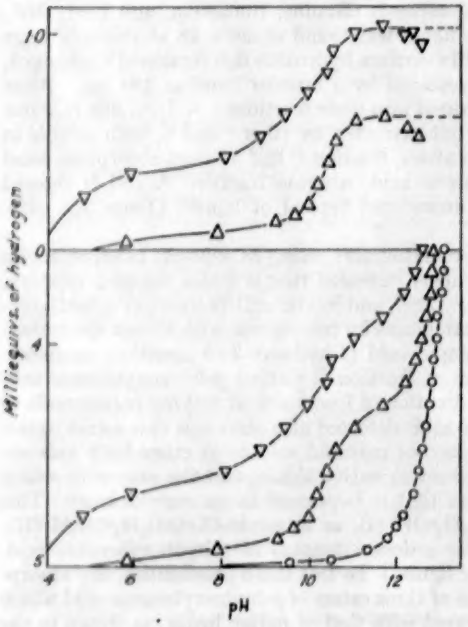


FIG. 2. *Hydrogen-binding curves (upper curves), and titration curves (lower curves), of aspen native lignin* (300 *mg.*).

Upper curves: △ Lignin before hydrolysis; ▽ lignin after hydrolysis.

Lower curves: ○ Sodium hydroxide (5 milliequivs.); △ with lignin before hydrolysis; ▽ with lignin after hydrolysis.

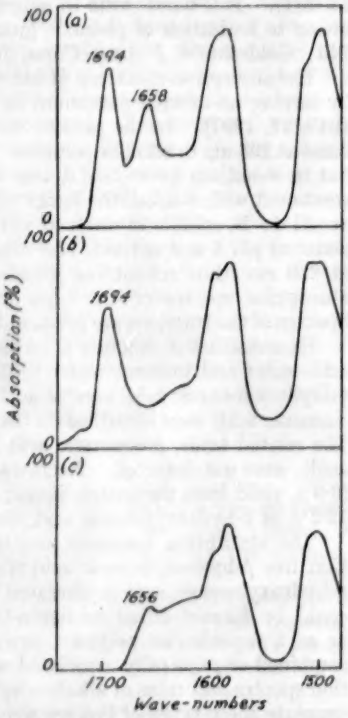


FIG. 3. *Infrared spectra of aspen native lignin in dioxan* (*c*, 10·0).

(*a*) Aspen native lignin.

(*b*) Aspen native lignin reduced by sodium borohydride.

(*c*) Aspen native lignin hydrolysed in aqueous sodium hydroxide.

nucleus, and *p*-hydroxybenzoate esters of phenolic groups of lignin would presumably show a similar shift. Since native lignin does not exhibit this shift, it is probable that the *p*-hydroxybenzoic acid molecules are linked individually by ester linkages of type I to

aliphatic hydroxyl groups of the lignin molecule. The rate of hydrolysis of the various compounds tends to confirm this suggestion. Hydrolysis of aspen native lignin in N-sodium hydroxide, measured spectrophotometrically, consists of a rapid stage (half-reaction time, 39 min.) ending at 69% hydrolysis, and a slow stage resulting in total hydrolysis in about 24 hours. The Table shows that this rate of hydrolysis is approached most closely by methyl *p*-hydroxybenzoate. The slower hydrolysis of lignin may be a consequence of its high molecular weight and the inaccessibility of some of its ester linkages.

The type of linkage postulated received confirmation from the titration curves of aspen native lignin, in the early and in the final stages of alkaline hydrolysis (Fig. 2). The inflexion at pH 11·5 denotes commencement of the process, phenoxide + H^+ ⟶ phenol; and the "hydrogen-binding curves" at this point (Parke and Davis, *Analyt. Chem.*, 1954, **26**, 642) measure the total acidic groups (phenolic and carboxylic) present. As lignin separated at about pH 10·4, the dissociation constants of the phenolic groups cannot be derived from the titration curves. Since precipitation of lignin is completed by pH 7, and since the phenolic acids hydrolysed from the lignin are still in solution, the hydrogen-binding curves in this region measure the free carboxylic groups present. The free *p*-hydroxybenzoic acid was also determined spectrophotometrically. The resulting analysis of hydrogen-binding groups is shown below in milliequivalents per g. of lignin :

	Phenolic groups	Carboxylic groups	Free *p*-hydroxybenzoic acid
After 15 min. in N-NaOH	1·8	0·2	0·1
After 24 hr. in N-NaOH	2·1	1·2	0·9
Increase on hydrolysis	0·3	1·0	0·8

Thus there is initially one equivalent of phenolic hydroxyl per 550 g. of lignin, and half of this is in *p*-hydroxybenzoate groups. The increase in free phenolic groups on hydrolysis is small, confirming that the hydroxyl groups involved in esterification are mostly aliphatic. The increase in carboxyl groups on hydrolysis exceeds the *p*-hydroxybenzoic acid released; this may be due to the presence of acetate, derived from acetaldehyde split off the lignin (unpublished work).

The infrared absorption spectrum of aspen lignin in the 5·5—6·5-μ region (Fig. 3) confirms the presence of *p*-hydroxybenzoate groups. There are two bands due to carbonyl-stretching at 1694 and 1658 cm.$^{-1}$, and also two doublets in the regions of 1600 and 1500 cm.$^{-1}$ which are characteristic of phenyl nuclei. The 1694- and 1658-cm.$^{-1}$ bands were each selectively eliminated, the former by alkaline hydrolysis in N-sodium hydroxide, and the latter by reduction with sodium borohydride in 0·01N-sodium hydroxide. This suggests that the 1694-cm.$^{-1}$ band is due to an ester-carbonyl, and the 1658-cm.$^{-1}$ band to an aldehyde- or ketone-carbonyl group. A study of the spectra of analogous simple substances confirms these assignments. The carbonyl-stretching bands of methyl *p*-hydroxybenzoate, acetovanillone, 4-hydroxy-3-methoxycinnamaldehyde, and 3 : 4-dimethoxycinnamaldehyde were at 1694, 1657, 1660, and 1661 cm.$^{-1}$, respectively.

Native lignin is only one of several fractions in the cold-alcoholic extract of wood. The ether-soluble fraction, rejected during isolation of native lignin, was found to resemble native lignin closely in its ultraviolet absorption in 0·01N-sodium hydroxide, suggesting that it also contains *p*-hydroxybenzoate groups. In addition, the residual wood, after exhaustive extraction with alcohol, gave 1·4% of *p*-hydroxybenzoic acid when boiled with N-sodium hydroxide. In this respect, as in others (Brauns, *J. Amer. Chem. Soc.*, 1939, **61**, 2120), the ether-soluble, the alcohol-soluble, and the insoluble fraction of lignin resemble one another so much as to suggest a common origin in the plant. The identification of *p*-hydroxybenzoate groups represents the first demonstration of a methoxyl-free aromatic nucleus in aspen lignin.

Experimental

Infrared spectra were measured on a single-beam spectrometer in dioxan solutions (10% for lignin, 7% for model substances) of 0·01-mm. thickness between sodium chloride plates.

Native Lignin.—Newly felled aspen branches (6″ diam.) were stripped of bark, phloem, and

pith, immediately reduced to sawdust, and stored at −25° until used. Sawdust (1 kg.) was continuously extracted with cold methanol, and the extract distilled under reduced pressure, leaving an aqueous suspension of toffee-like solid. The solid was washed, dried *in vacuo*, and extracted with methanol (dried; 75 c.c.), leaving a residue (discarded). The resulting solution was run slowly into ether (dried, peroxide-free; 2·5 l.) with vigorous stirring. Lignin, precipitated as a pale cream-coloured powder, was centrifuged, washed with ether, and stored in a current of dry air until free from solvent (yield, 5·5 g.). The product, readily soluble in methanol and aqueous alkali, became partly insoluble in methanol after prolonged drying *in vacuo* (Found, in dried material: OMe, 21·7%).

Hydrolysis of Lignin.—Lignin (100 mg.) in 2·3N-methanolic potassium hydroxide (5 c.c.) was kept for 24 hr., then diluted with methanol (5 c.c.) and poured into water (80 c.c.) containing acetic acid (3 c.c.). The precipitate was centrifuged (fraction A), and the supernatant liquid was extracted with ether (giving fractions B and C). The ultraviolet absorption of each fraction was measured in N-sodium hydroxide.

In an experiment with lignin (300 mg.), fraction C, after evaporation and recrystallisation from hot water (1·5 c.c.) yielded *p*-hydroxybenzoic acid (20·6 mg.), m. p. 208—210°. Vacuum-sublimation raised the m. p. to 215—216° (authentic m. p. 216—217°; mixed m. p. 215—217°) (Found: C, 61·1; H, 4·4. Calc. for $C_7H_6O_3$: C, 60·9; H, 4·4%).

Paper Chromatograms.—The descending method on Whatman No. 1 paper was used. For detection of spots, chromatograms were sprayed with diazotised *p*-nitroaniline in sodium acetate (Swain, *Biochem. J.*, 1953, **53**, 200).

Hydrolysis Rates.—These were measured spectrophotometrically by the increase in extinction at 280 mμ (*p*-acetoxybenzoic acid), or by the decrease in extinction at 304 mμ [methyl *p*-hydroxybenzoate, 4-(*p*-hydroxybenzoyloxy)benzoic acid, lignin].

Hydrolysis of p-*acetoxybenzoic acid*, m. p. 187—190°; $c = 5 \times 10^{-4}$ g./100 c.c. in 0·01N-sodium hydroxide.

Time (sec.)	50	100	150	200	350
Hydrolysis (%)	34·5	64·5	85·6	95·5	100

Hydrolysis of 4-(p-*hydroxybenzoyloxy*)*benzoic acid* (Fischer and Freudenburg, *Annalen*, 1910, **372**, 47), m. p. 270°; $c = 7 \times 10^{-4}$ g./100 c.c. in N-sodium hydroxide.

Time (min.)	4	10	18	35	95
Hydrolysis (%)	41·2	77·4	86·3	94·4	100

Hydrolysis of methyl p-*hydroxybenzoate*, m. p. 124—128°; $c = 7 \times 10^{-4}$ g./100 c.c. in N-sodium hydroxide.

Time (min.)	5	10	18	35	95
Hydrolysis (%)	19·3	35·3	54·6	33·0	100

Hydrolysis of aspen native lignin, $c = 2{\cdot}3 \times 10^{-3}$ g./100 c.c. in N-sodium hydroxide.

Time (min.)	5	12	25	49	95	153	180	1200
Hydrolysis (%)	6·8	14·4	27·3	41·7	58·5	66·8	68·2	100

Titration Curves.—These were obtained using a "Doran alkacid" sealed glass electrode, a calomel microelectrode with wick-type liquid junction, and a "Cambridge portable" pH-meter. Lignin (300 mg.), N-sodium hydroxide (5 c.c.), and water (2 c.c.) were titrated with N-hydrochloric acid, admitted through an immersed capillary into a cell with a magnetic stirrer. After each addition of acid, precipitated lignin was allowed to redissolve before a reading was taken. At pH 10·4, lignin failed to redissolve.

Hydrolysis of Wood.—Aspen wood, after exhaustive extraction with cold methanol, was reduced in a ball-mill to pass a 200-mesh sieve. Powdered wood (200 mg.) in N-sodium hydroxide (200 c.c.) was shaken at room temperature or boiled under reflux. Samples were withdrawn at stated times and centrifuged, and the supernatant liquids (15 c.c. each) were shaken with ether (100 c.c.) containing acetic acid (2 c.c.). The ether extracts were washed once with water (100 c.c.) and extracted with N-sodium hydroxide (10 c.c.). The *p*-hydroxybenzoic acid contents were measured by the extinction at 280 mμ. The standard recovery was determined on pure *p*-hydroxybenzoic acid. Yields at room temperature were 0·38 and 0·72% after 4 and 24 hr. respectively.

Extraction of wood at 100°.

Time (min.)	15	30	60	120
Yield of *p*-hydroxybenzoic acid (%)	1·23	1·32	1·39	1·44

The author thanks Dr. T. Swain for advice in obtaining infrared spectra, and Messrs. J. E. Ayers and H. J. Moore gave technical assistance. This work forms part of the programme of the Food Investigation Organisation of the Department of Scientific and Industrial Research.

LOW TEMPERATURE RESEARCH STATION, CAMBRIDGE. [*Received, February 21st*, 1955.]

The Cyclodehydration of Anils. Part I. Kinetics of Cyclodehydration of 2-Anilino- and 2-p-Toluidino-pent-2-en-4-one in Sulphuric Acid.

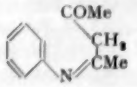
By T. G. BONNER, M. P. THORNE, and J. M. WILKINS.

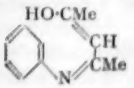
[Reprint Order No. 6169.]

The rates of cyclodehydration of 2-anilino- and 2-*p*-toluidino-pent-2-en-4-one have been measured in aqueous sulphuric acid in the range 84·5—97·3% H_2SO_4. The first-order rate constants (k_1) for a fixed initial 0·1M-concentration of condensation product are related to the acidity function, H_0, by Hammett's equation $\log k_1 + H_0 = \text{constant}$. An approximately linear relation is found between k_1 and the molar ratio $[H_2SO_4]/[HSO_4^-]$. This relation also applies to the rate constants determined in ammonium sulphate–sulphuric acid if it is assumed that the NH_4^+ ion has a solvation number of 1 in sulphuric acid.

THE formation of 2 : 4-dimethylquinolines when the condensation products of acetylacetone and primary arylamines are heated in sulphuric acid was first investigated by Combes (*Compt. rend.*, 1887, **106**, 142; *Bull. Soc. chim.*, 1888, **49**, 90). The influence of substituent groups in the aromatic nucleus on this cyclodehydration reaction was examined by Turner and Roberts (*J.*, 1927, 1836), and their results, together with subsequent work on cyclodehydration, have been summarised by Bradsher (*Chem. Rev.*, 1946, **38**, 447).

The condensation products are usually represented as tautomeric ketimine (I or II) and enamine (III) structures; *e.g.*, the last is 2-anilinopent-2-en-4-one. From a study of the


(I)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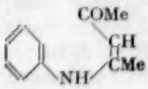
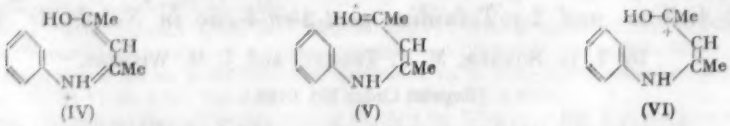

(III)

molecular refractivity of this anil, using both the pure compound and its solution in methylnaphthalene, von Auwers and Susemihl (*Ber.*, 1930, **63**, 1072) obtained exaltations of 3·5 for the pure compound and 3·35 for the solution above the value calculated for structure (III). They concluded that the anil has this structure, since there exists conjugation between the C=C bond and C=O group and between the nitrogen atom and the benzene ring. However, comparison of the calculated molecular refractivities of the forms (II) and (III) shows that they differ only in the contribution of the nitrogen and the oxygen atoms which are differently bound in the two structures. The molecular refractivity values for these contributions are shown below [values taken from von Auwers and Susemihl (*loc. cit.*) and Gilman's "Organic Chemistry," John Wiley & Sons, Ltd., 2nd Edn., 1943, Vol. II, p. 1751]. The difference of only 0·135 therefore does not permit a decision between the two structures.

$C_6H_5{\cdot}NH{\cdot}C(CH_3){:}CH{\cdot}C(CH_3){=}O$	Secondary N atom	2·499	4·710
	=O	2·211	
$C_6H_5{\cdot}N{:}C(CH_3){\cdot}CH{:}C(CH_3){\cdot}OH$	–N=	3·05	4·575
	–O–	1·525	

The ketimine structure has been proposed in cases where failure to cyclise under the usual conditions has been observed; *e.g.*, since the products from aniline and formylacetone (Thielpape, *Ber.*, 1922, **55**, 127) and from *p*- and *o*-chloroaniline and acetylacetone (Turner and Roberts, *loc. cit.*) could not be cyclised in acidic media, it was suggested that they exist in the *trans*-form of the ketimine, which is sterically unsuited to cyclisation. Edwards and Petrow (*J.*, 1954, 2853) recently dealt with this point and from infrared-spectral studies concluded that the products from *o*-, *m*-, and *p*-chloroaniline and acetylacetone are in the ketimine form; of these only the *m*-compound cyclises in sulphuric acid (Turner and Roberts, *loc. cit.*).

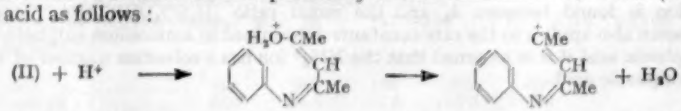
It is reasonable to assume that in the acid media employed for cyclodehydration the reacting form is cationic, and the same cationic resonance structures (IV)—(VI) can be derived from structure (II) or (III) by proton uptake.



(IV) (V) (VI)

Similar cationic structures in other cyclisations in acid media have been suggested by Petrow (*J.*, 1942, **693**), Berliner (*J. Amer. Chem. Soc.*, 1944, **66**, 533), and Morley and Simpson (*J.*, 1948, 2024).

An alternative but more remote possibility is that the anil in the form (II) ionises in sulphuric acid as follows :



(VII)

A decision between the alternative cationic species represented by (IV)—(VI) and (VII) can be made by examining the relations between the rate constant of the cyclodehydration and Hammett's acidity function H_0 and the J_0 function defined by Gold and Hawes (*J.*, 1951, 2102). Hammett and Deyrup (*J. Amer. Chem. Soc.*, 1932, **54**, 2721) showed that if a reaction in sulphuric acid is of the first order and the reacting species is formed by uptake of a single proton from the medium without further modification of the cation which results, then, provided there is only a relatively small fraction of the compound present in its cationic form, the experimental rate constant k_1 and the acidity function H_0 are related by the equation $\log k_1 + H_0 = \text{constant}$, where $H = -\log \alpha_{H^+} f_B / f_{BH^+} = pK + \log [B]/[BH^+]$, K representing the acid dissociation constant, and $[B]$ and $[BH^+]$ the concentration of un-ionised and ionised form of a base indicator ionising in the medium by simple proton uptake. This is in effect equivalent to demonstrating the constancy of the sum of $\log k_1$ and the logarithm of the ionisation ratio $[B]/[BH^+]$ of a simple basic indicator ionising over the range of media for which kinetic data are obtainable.

If on the other hand the cyclisation occurs in the cationic species represented by structure (VII), then a similar type of relation can be deduced between k and the ionisation ratio $[ROH]/[R^+]$ of a triphenylmethanol-type indicator which ionises according to the sequence

$$ROH \overset{H^+}{\rightleftharpoons} ROH_2^+ \rightleftharpoons R^+ + H_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Let $[A]_T$ represent the concentration of the total amount of "anil" present, $[A^+]$ that present as the cation (VII), and $[A]$ that of the residual "anil." The theoretical rate equation (for a first-order reaction) is given by $k_0[A^+]f_{A^+}/f_{tr}$, where f_{tr} is the activity coefficient of the transition complex. Assuming that the activity coefficient ratio f_{A^+}/f_{tr} is constant over the range of media investigated, and equating with the experimental rate equation, we have :

$$k_1[A]_T = k[A^+] \text{ where } k = k_0 f_{A^+}/f_{tr} \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

or

$$\log k_1 + \log [A]_T/[A^+] = \log k \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

For alcohols ionising in the form of equation (1) it has been shown (Murray and Williams, *J.*, 1950, 3318) that the difference between the logarithms of the ionisation ratios of two such compounds over narrow ranges of sulphuric acid–water media is a constant. If the same relation holds for an " anil " ionising as in (1) we can write :

$$\log [A]/[A^+] - \log [ROH]/[R^+] = \text{constant (independent of medium)} \quad . \quad (4)$$

where ROH represents a triphenylmethanol indicator ionising in the range of media in which the rates of cyclisation have been measured. If the extent of conversion of the compound A into its cation A^+ is very small, *i.e.*, $[A^+] \ll [A]$ so that [A] is approximately the same as $[A]_T$, we have by combining (3) and (4) :

$$\log k_1 + \log [ROH]/[R^+] = \text{constant} \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

A correlation of this kind between the rate of nitration of benzene and the ionisation ratio for 4 : 4′ : 4″-trinitrotriphenylmethanol in sulphuric acid, found by Westheimer and

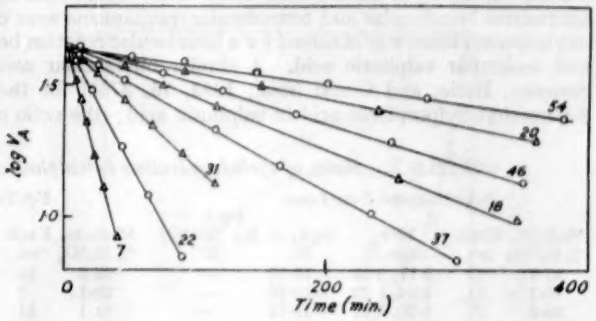


FIG. 1.

○ 2-*Anilinopent-2-en-4-one.*
△ 2-p-*Toluidinopent-2-en-4-one.*

Kharasch (*J. Amer. Chem. Soc.*, **1946**, **68**, 1871), provided evidence that the nitric acid ionised according to (1) to produce the nitronium NO_2^+ ion. A more general form of equation (5) is :

$$\log k_1 + J_0 = \text{constant} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where J_0, as defined by Gold and Hawes (*loc. cit.*), is given by $J = -pK_{ROH} + \log [ROH]/[R^+]$. Equation (6) has been shown to apply to the nitration of the p-$C_6H_4Me{\cdot}NMe_3^+$ ion in sulphuric acid (Lowen, Murray, and Williams, *J.*, 1950, 3318) and to the decarbonylation of triphenylacetic acid in sulphuric acid (Deno and Taft, *J. Amer. Chem. Soc.*, **1954**, **76**, 244, from results obtained by Dittmar, *J. Phys. Chem.*, 1929, **33**, 533). In the present paper, equation (5) is preferred to equation (6) as a test of this mechanism, since an agreed scale of J_0 values over a sufficient range of media is not yet available (see Williams and Bevan, *Chem. and Ind.*, 1955, 171, and Gold, *ibid.*, p. 172).

Kinetics of the Cyclodehydration.—The rates of conversion of 2-anilino- and of 2-*p*-toluidino-pent-2-en-4-one into 2 : 4-dimethyl- and 2 : 4 : 6-trimethyl-quinoline in aqueous sulphuric acid were followed by hydrolysis of the unchanged compound at known intervals of time to the aromatic amine and acetylacetone, and colorimetric estimation of the latter by conversion into ferric acetylacetone in aqueous acid. Excellent first-order rate constants were obtained for both compounds in the range of media studied as shown in Fig. 1. The rate constant depends to a slight extent on the initial concentration of the " anil "; this is a feature of other reactions in sulphuric acid, *e.g.*, nitration, and will form the subject of a separate study. All results quoted in this paper have been obtained with an initial 0·1M-concentration of organic reactant. The results for the anilino- and the *p*-toluidino-compounds are shown in Table 1. The H_0 values were taken from a curve obtained by plotting the experimental H_0 values (quoted by Deno and Taft, *loc. cit.*) against percentage of sulphuric acid, and the log [ROH]/[R^+] values were similarly obtained from the results

of the investigation of the ionisation of 4 : 4′ : 4″-trinitrotriphenylmethanol (Murray and Williams, *loc. cit.*). It is clear that the ($\log k + H_0$) values are reasonably constant for both compounds, while there is a marked variation in the ($\log k + \log [ROH]/[R^+]$) values. It can be concluded that the products cyclise in the form of simple cationic structures resulting from uptake of a single proton without further change in the ionic species.

First-order rate constants were obtained in the decarbonylation of aromatic aldehydes (Schubert and Zahler, *J. Amer. Chem. Soc.*, **1954**, **76**, 1) and in the decarboxylation of aromatic acids (Schubert, Donohue, and Gardner, *ibid.*, p. 9) in sulphuric acid, but the authors concluded that the Hammett unimolecular mechanism does not apply to these reactions. In both reactions studied, extensive conversion of the aromatic compound (B) into its conjugate acid (BH^+) occurs in relatively aqueous acids (60—80% sulphuric acid) and a modified form of the Hammett equation was used, *viz.*,

$$\log k + H_0 - \log [B]/[B]_{stoich.} = \text{constant}$$

where [B] represents the concentration of un-ionised form and $[B]_{stoich.}$ the total concentration (all forms) of the aromatic compound. Since their results did not fit this equation, alternative bimolecular and termolecular mechanisms were considered and for the decarboxylation evidence was obtained for a bimolecular reaction between the aromatic compound and molecular sulphuric acid. A similar bimolecular mechanism was put forward by Sommer, Barie, and Gould (*ibid.*, **1953**, **75**, **3765**) for the formation of methane from β-trimethylsilylpropionic acid in sulphuric acid; the ratio of the first-order rate constant

TABLE 1. *Rates of cyclodehydration in sulphuric acid–water media.*

2-Anilinopent-2-en-4-one					2-*p*-Toluidinopent-2-en-4-one				
Medium, % H_2SO_4	Expt. no.	10^3k_1 (min.$^{-1}$)	$\log k_1 + H_0$	$\log k +$ log [ROH]/[R^+]	Medium, % H_2SO_4	Expt. no.	10^3k_1 (min.$^{-1}$)	$\log k_1 + H_0$	$\log k +$ log [ROH]/[R^+]
97·3	22	2·11, 2·09	−10·79	—	95·5	95	8·49, 8·45	− 9·89	—
95·7	71	1·24, 1·22	−10·76	—	93·1	7	4·29, 4·28	− 9·91	−2·57
95·5	97	1·20, 1·21	−10·74	—	91·1	11	2·12, 2·12	− 9·98	−2·32
95·2	26	1·14	−10·72	—	89·2	13	1·22, 1·23	−10·00	−2·05
93·3	37	0·614, 0·622	−10·77	−3·46	89·0	31	1·06, 1·05	−10·01	−2·02
91·2	46	0·343, 0·341	−10·79	−3·15	87·6	24	0·742, 0·741	−10·05	−1·83
89·2	75	0·211, 0·210	−10·77	−2·80	86·3	18	0·445, 0·450	−10·10	−1·63
88·6	54	0·166, 0·163	−10·80	−2·75	85·5	27	0·330, 0·330	−10·13	−1·50
					84·5	20	0·238, 0·239	−10·14	−1·32

for the evolution of methane to the concentration of molecular sulphuric acid was shown to be constant over the range 89—97% sulphuric acid, and Deno and Taft (*loc. cit.*) later established that the constancy of this ratio was maintained down to 85% sulphuric acid. There is no evidence of any such correlation in the cyclodehydration, and this particular bimolecular mechanism can be rejected for this reaction.

Relation between the Rate Constant and the Ratio $[H_2SO_4]/[HSO_4^-]$.—Brand (*J.*, 1950, 1002) has shown that Hammett's acidity function H_0 in the range 89—99·8% sulphuric acid can be calculated with the empirical equation

$$H_0 = -8{\cdot}36 + \log [HSO_4^-]/[H_2SO_4] \quad . \quad . \quad . \quad . \quad . \quad (7)$$

if the reaction

$$H_2O + H_2SO_4 = H_3O^+ + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

is assumed to be complete. Deno and Taft (*loc. cit.*) later showed that equation (7) is applicable in the range of media 83—89% sulphuric acid if a value of 50 is assigned to the equilibrium constant, K, of reaction (8). As a consequence of the validity of this method of calculating H_0 values, these authors conclude that the activity coefficient ratio $f_{H_3O^+}f_{HSO_4^-}/f_{H_2O}f_{H_2SO_4}$ is constant over the range 83—100% sulphuric acid. From the constancy of the $\log k_1 + H_0$ addition in the cyclodehydration, it follows that for this reaction

$$\log k_1 - \log [H_2SO_4]/[HSO_4^-] = \text{constant} \quad . \quad . \quad . \quad . \quad . \quad (9)$$

A simple derivation of equation (9) is possible from the following considerations. If the compound A is involved in the equilibrium

$$A + H_2SO_4 \rightleftharpoons AH^+ + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

with an equilibrium constant K' given by

$$K' = \frac{[AH^+][HSO_4^-]}{[A][H_2SO_4]} \frac{f_{AH^+}f_{HSO_4^-}}{f_A f_{H_2SO_4}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

then from equation (11) and the appropriate form of equation (3) in which $[A^+]$ is replaced by $[AH^+]$, assuming that $[AH^+] \ll [A]$ (*i.e.*, [A] is approximately equal to $[A]_T$), we have

$$k_1 = kK'[H_2SO_4]/[HSO_4^-] \times \text{constant} \quad . \quad . \quad . \quad . \quad . \quad (12)$$

since the activity coefficient term is similar to that for the equilibrium (8) and can be expected to show the same constancy. The direct relation between the rate constant, k_1, and the ratio $[H_2SO_4]/[HSO_4^-]$ indicated in equation (12) is evident in Fig. 2, in which

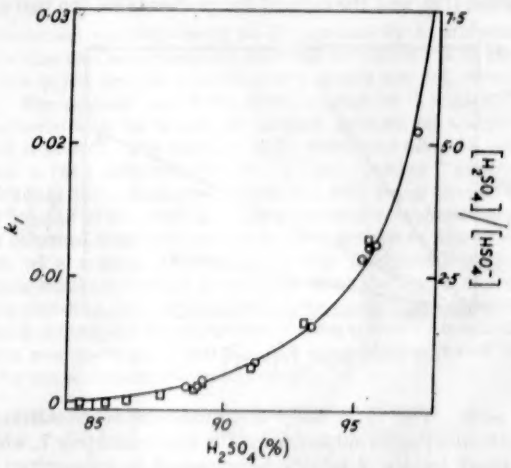


FIG. 2.
○ 2-*Anilinopent-2-en-4-one.*
□ 2-p-*Toluidinopent-2-en-4-one.*

the curve represents the variation of $[H_2SO_4]/[HSO_4^-]$ with percentage of sulphuric acid; the values of the rate constants for both condensation products plotted (on suitable ordinate scales) against the percentage of sulphuric acid in the media in which they are determined lie very close to the curve. No parallelism is found with the curves of the variation of $[H_2SO_4]$ or $[HSO_4^-]$ with the percentage of sulphuric acid.

A more stringent test of equation (12) is the demonstration that the plot of k_1 against $[H_2SO_4]/[HSO_4^-]$ is a straight line. This is shown in Fig. 3 and for both compounds reasonable linearity is evident. Also included in this Figure is the plot of k_1 against $[H_2SO_4]/[HSO_4^-]$ for the cyclodehydration of the *p*-toluidino-compound in water-free $(NH_4)_2SO_4$–H_2SO_4 media. The relevant results are shown in Table 2, where $[H_2SO_4]_T$ represents the stoicheiometric concentration of sulphuric acid, and $[H_2SO_4]$ the residual molecular sulphuric acid concentration. Each mole of ammonium sulphate requires 1 mole of sulphuric acid according to the equation $(NH_4)_2SO_4 + H_2SO_4 = 2NH_4^+ + 2HSO_4^-$. Although no simple correlation is found between k_1 and $[H_2SO_4]/[HSO_4^-]$ if this represents the sole interaction, yet the linear relation is obeyed if it is assumed that each ammonium ion binds 1 molecule of sulphuric acid by solvation. Evidence that this solvation occurs is provided by the freezing-point–composition data for $(NH_4)_2SO_4$–H_2SO_4 mixtures (Kendall and London, *J. Amer. Chem. Soc.*, 1920, **42**, 2135), which indicate the existence of a stable compound $(NH_4)_2SO_4,3H_2SO_4$, and the interpretation of the depression of freezing point

of pure sulphuric acid by small amounts of ammonium sulphate by Gillespie, Hughes, and Ingold (*J.*, 1950, 2487) in terms of a solvation number of unity for the ammonium ion.

The constancy of the term in the last column of Table 2 is another expression of the

TABLE 2. *Rates of cyclodehydration of* 2-p-*toluidinopent-2-en-one in* $(NH_4)_2SO_4$–H_2SO_4 *media.* (All concns. in moles/l.)

$(NH_4)_2SO_4$	k_1	$[HSO_4^-]$	$[H_2SO_4]_T$	$[H_2SO_4]$	$\frac{[H_2SO_4]}{[HSO_4^-]}$	$\log k_1 - \log [H_2SO_4]/HSO_4^-]$
1	0·131	2	17·42	14·42	7·21	−1·74
2	0·0554	4	16·14	10·14	2·54	−1·67
2·5	0·0314	5	15·47	7·97	1·59	−1·70
3	0·0172	6	14·80	5·80	0·97	−1·75
4	0·00298	8	13·36	1·36	0·17	−1·76

relation given by equation (12) and shows in effect that the Hammett equation is obeyed although it cannot be tested directly since H_0 values have not been determined for $(NH_4)_2SO_4$–H_2SO_4 media.

The gradient of each line in Fig. 3 represents the product of the constant terms in equation (12), and the ratio of the gradients for the two anils is the ratio of the kK products

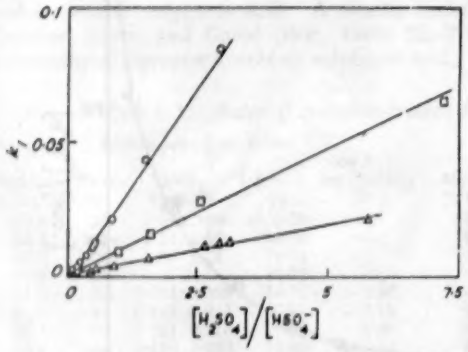


FIG. 3.
○ 2-p-*Toluidinopent-2-en-4-one in* H_2SO_4–H_2O.
△ 2-*Anilinopent-2-en-4-one in* H_2SO_4–H_2O.
□ 2-p-*Toluidinopent-2-en-4-one in* $(NH_4)_2SO_4$–H_2SO_4 ($k_1 \times 0·5$).

for each. The ratio kK(*p*-toluidino-compound)/kK(anilino-compound) obtained for the results in aqueous sulphuric acid is approximately 7, while the same ratio, from the results obtained for the *p*-toluidino-compound in ammonium sulphate–sulphuric acid, is *ca.* 5. The *p*-toluidino-compound cyclises more rapidly than the anilino-compound as a result of (i) the activating effect of the methyl group at the *meta*-position where ring closure occurs and (ii) the greater basicity of the nitrogen atom which is in the *para*-position to the methyl group. The rate of electrophilic substitution in aromatic compounds at the *meta*-position to a methyl group is about 2·5—3 times faster than in the unsubstituted benzene ring; this would account for about half the kK ratio found experimentally, the remainder presumably being the result of the greater basicity of the *p*-toluidino-compound.

EXPERIMENTAL

Materials.—Aniline and acetylacetone were distilled before use, and *p*-toluidine was crystallised twice from aqueous alcohol. The condensation products were prepared by Turner and Roberts's method (*loc. cit.*) and were recrystallised twice from light petroleum (b. p. 40—60°); 2-anilinopent-2-en-4-one had m. p. 50—52°; 2-*p*-toluidinopent-2-en-4-one had m. p. 65—66°.

Media.—Sulphuric acid–water mixtures were prepared by adding water or redistilled oleum to "AnalaR" concentrated sulphuric acid and standardised against N-sodium hydroxide referred through N-hydrochloric acid to potassium iodate. 100% Sulphuric acid was obtained by adjustment of a weak oleum to maximum freezing point. Water-free ammonium sulphate–sulphuric acid mixtures were prepared directly for each kinetic experiment by weighing the required amount of ammonium sulphate into a tared 50-ml. volumetric flask, adding 100%

sulphuric acid to dissolve the solid, and making up to the mark at 25°; the flask was then reweighed to obtain the weight of pure sulphuric acid present.

Conversion into Quinoline Compounds.—To establish that the cyclodehydration is practically quantitative under the conditions used for rate measurements, 1 g. of 2-anilinopent-2-en-4-one was rapidly dissolved in 10 ml. of 97·9% sulphuric acid (this corresponds to 5 times the concentration of organic reactant used in kinetic experiments) and kept at room temperature for 2 hr. The solution was poured into ice-cold water (100 ml.) and left for 2 hr. to ensure complete hydrolysis. The solution at 5° was treated with an ice-cold solution of sodium nitrite (0·05 g.) in water (5 ml.) to diazotise any aniline resulting from the hydrolysis, and then warmed to convert the diazonium salt into phenol. After cooling, sodium hydroxide (15 g.) was added to make the solution alkaline. The 2 : 4-dimethylquinoline was extracted with ether, and the ether extracts were washed with water and dried (Na_2SO_4). After filtration and evaporation, the crude product was obtained as a yellow liquid (yield 92%) (Found : C, 82·9; H, 7·2; N, 9·0. Calc. for $C_{11}H_{11}N$: C, 84·0; H, 7·05; N, 8·9%)

In a similar experiment, 2-*p*-toluidinopent-2-en-4-one (1 g.) was dissolved in a solution (10 ml.) of 1 mole/l. of ammonium sulphate in 100% sulphuric acid and kept for 2 hr. 2 : 4 : 6-Trimethylquinoline was recovered in 93% yield by the method described above (m. p. of crude product 40—41·5°; m. p. of pure compound 43—45°) (Found : C, 84·2; H, 8·0; N, 7·6. Calc. for $C_{12}H_{13}N$: C, 84·2; H, 7·65; N, 8·2%).

Analytical Method.—The condensation products could be determined by hydrolysis in *ca.* 2N-sulphuric acid to the aromatic amine and acetylacetone, followed by conversion of the latter into its soluble ferric complex; this is red and its solution obeys Beer's law (cf. Bonner and Thorne, *Analyst*, 1954, **79**, 759). The reagent is a 6·5% w/w solution of "AnalaR" ferric ammonium sulphate in 0·1N-sulphuric acid to which an aliquot portion of acetylacetone (1—2·5 mg.) in 0·1N-sulphuric acid is added. The colour is fully developed after 15 min., and the optical density of the solution is then determined on a "Hilger Spekker" photoelectric absorptiometer, a sodium filament lamp and a blue-green filter (No. 603) being used to confine the incident light to a wavelength band of 4700—5000 Å. The amount of acetylacetone present is read off from a standard curve obtained from measurements on solutions of known concentration. No interference occurs with aniline, *p*-toluidine, or the corresponding quinoline compounds, and the effect of sodium sulphate present in solutions from the kinetic experiments can be eliminated by obtaining the standard curve with acetylacetone solutions containing this salt. The results of analysis of pure 2-anilinopent-2-en-4-one are shown below. After hydrolysis with 2N-sulphuric acid each solution was made up to 500 ml., and the acidity adjusted to 0·1N. A suitable aliquot part was taken for the acetylacetone determination.

Reactant taken (g.)	Aliquot taken (ml.)	Acetylacetone in aliquot : Calc. (mg.)	Found (mg.)
0·2222	5	1·27	1·27
0·1295	10	1·48	1·50
0·0796	15	1·36	1·37

Procedure for Measuring the Rate of Cyclodehydration.—Kinetic measurements were carried out at 25° in a thermostat controlled to ±0·02°. The reaction vessel was a 100-ml. round-bottomed flask with a B24 neck. The organic reactant was weighed into a B24 socket cap, the amount taken providing a 0·1M-solution when dissolved in 50 ml. of the medium. The medium, previously made up to the mark in a tared 50-ml. volumetric flask at 25°, was transferred to the reaction vessel; 30 sec. were allowed for drainage, and the flask was reweighed to allow a correction to be made for incomplete transfer. To start the reaction, the reaction vessel was removed from the thermostat, and the filled socket cap inserted. The medium and reactant were brought into contact at zero time by vigorous shaking, and after complete dissolution had occurred (1—2 min.) the flask was returned to the thermostat. Air bubbles formed during the shaking were rapidly removed by replacing the socket cap with a B24 cone connected to a suction pump. As soon as the liquid was clear (1—2 min.) the cone and pump were detached and the flask was restoppered. Six to eight 2-ml. samples were taken from the reaction mixture in the course of a run. Each sample was drawn into 2-ml. pipette, having a wide delivery jet and previously standardised for delivery of sulphuric acid, and run into 20 ml. of ice-cold water. This dilution stopped the reaction and also provided an approximately 2N-sulphuric acid. After the mixture had been kept for 2 hr. at room temperature to ensure complete hydrolysis of unconverted anil, 2·5 g. of pellet sodium hydroxide were added to the ice-cold solution to neutralise the bulk of the acid present. The solution was finally adjusted to neutrality by successive titration with

N-sodium hydroxide, N-sulphuric acid, and 0·1N-sodium hydroxide (B.D.H. Universal Indicator paper); the proximity of the end-point is indicated by the separation of the quinoline. 5 Ml. of N-sulphuric acid were added, and the solution filtered into a 50-ml. volumetric flask and made up to the mark with washings. The solution, now 0·1N with respect to sulphuric acid, was analysed by adding a 5-, 10-, or 15-ml. aliquot portion to 5 ml. of the ferric ammonium sulphate reagent and dilution to a final volume of 20 ml. with 0·1N-sulphuric acid. The optical density was measured as described above against a blank prepared in the same way from 2 ml. of the pure medium. Reactions were followed up to about 80% change. Rate constants were obtained from the first-order rate equation $k_1 t = 2{\cdot}303\{\log a - \log(a-x)\}$; k_1 (min.$^{-1}$), was obtained graphically from the plot of log V_a against t, where V_a is the volume of the standard acetylacetone solution equivalent to the amount of acetylacetone in each 2-ml. aliquot portion of the reaction mixture removed. Duplicate determinations were carried out and these rarely differed by more than 1%.

Test for Surface Catalysis Effects.—The rate of cyclodehydration of 2-anilinopent-2-en-4-one in 95·5% sulphuric acid at 25° was unaltered within the limits of experimental accuracy by the addition of a quantity of small glass balls (with and without this addition, rate constant = 0·0123 and 0·0121 min.$^{-1}$, respectively). The reaction thus occurs entirely in the homogeneous liquid phase.

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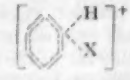
The Cyclodehydration of Anils. Part II. The Hydrogen Isotope Effect in the Cyclodehydration of 2-Anilinopent-2-en-4-one.*

By T. G. BONNER and J. M. WILKINS.

[Reprint Order No. 6170.]

The ratio of the rates of cyclodehydration of 2-(2 : 4 : 6-trideuteroanilino)-pent-2-en-4-one and its protium analogue is found to be approximately 2 : 3 in both 95·5% and 89·2% sulphuric acid–water. It is suggested that although fission of the C–H bond is not the kinetically decisive factor in the cyclodehydration, some weakening of the bond occurs in the rate-determining step.

IN a detailed discussion of the mechanism of aromatic electrophilic substitution, Melander (*Arkiv Kemi*, 1950, **2**, 211) considered the hydrogen isotope effect in the two alternative S_E2 processes—the single step replacement with the activated complex (I), and the two-stage process with an intermediate addition compound (II) regarded as having rather greater stability than the activated complex. In (I) the π-electrons of the benzene ring do not take part in the formation of π-bonds, although they may be polarised by the positive charge;

(I)  + (II)

but in (II), two of these electrons are used for the addition of the cation resulting in the appearance of four bonds of the sp^3 type at the nuclear carbon atom. If, experimentally, identical rates of substitution for hydrogen isotopes are found, this implies that the stepwise reaction occurs with a rate-determining first step, since this step does not involve hydrogen loss; if a substantially slower rate is observed for the heavy isotope the substitution may occur either by the stepwise reaction with the second step rate-determining, or by the single-step replacement. The isotopic rate ratio k_T/k_H for the rates of replacement of tritium and protium may be found to have any value from unity to about 0·05. In nitration and bromination experiments, Melander obtained minimum values of 0·74—0·85 for k_T/k_H and concluded that these results established that the hydrogen loss in both substitution reactions was kinetically insignificant. The result for the nitration was confirmed by Bonner, Bowyer, and Williams (*J.*, 1953, 2650) who obtained values of 0·99

* Part I, preceding paper.

and 0·95 for k_D/k_H by direct determination of the rates of nitration of nitrobenzene and pentadeuteronitrobenzene in sulphuric acid solution. For sulphonation a significantly lower isotope ratio of 0·55 for k_T/k_H has been reported by Berglund-Larsson and Melander (*Arkiv Kemi*, 1953, **6**, 219) and their interpretation of this result favours the step-wise reaction with the second step rate-determining.

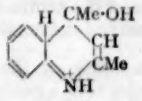
Rates of cyclodehydration at 25°.

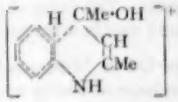
Initial concn. of organic reactant 0·1M. k in min.$^{-1}$.

Medium, % H_2SO_4	Expt. no.	k_H	Expt. no.	k_D	k_D/k_H
95·7	71	0·0124, 0·0122	72	0·00811, 0·00811	0·66
89·2	75	0·00210, 0·00211	78	0·00148, 0·00149	0·71

The Isotope Effect in Cyclodehydration.—The ratio k_D/k_H in cyclodehydration was determined by measuring the rates of conversion of 2-anilino-(k_H) and 2-(2 : 4 : 6-trideuteroanilino)-pent-2-en-4-one (k_D) to the corresponding quinoline derivatives by the method described in Part I. The first-order rate constants obtained are shown in the Table.

A definite isotope effect is evident, but the ratio is sufficiently close to unity to exclude the possibility that the fission of the C–H bond is the sole rate-determining factor. The reaction is an intramolecular electrophilic substitution within the cation formed by proton uptake from the medium and differs from a bimolecular electrophilic substitution in that the formation of the product requires the elimination of a molecule of water instead of a proton. In a mechanism corresponding to the formation of the intermediate addition compound (II) the cation would assume the structure (III). Elimination of a molecule of

(III) 



(IV)

water from this intermediate in strongly acidic media should be rapid. Further, if interaction with sulphuric acid were kinetically significant, then the simple relation between the rate constant and the ratio $[H_2SO_4]/[HSO_4^-]$ found experimentally (Part I), *viz.*, k = const.$[H_2SO_4]/[HSO_4^-]$, could hardly be expected; the derivation of this equation assumes that the only interaction between the organic reactant (A) and the solvent species is that involved in the equilibrium, $A + H_2SO_4 \rightleftharpoons AH^+ + HSO_4^-$. It follows that if the reaction occurs by a two-step process through the intermediate compound (III), it is the formation of this compound which is the rate-determining step, and the small isotope effect must be accepted as a feature of this mechanism. The alternative single-step mechanism represented by the transition complex (IV) is less likely since the difference in zero-point energies of the C–H and C–D bonds should lead to a much lower k_D/k_H ratio than that found experimentally. The effect might not be so pronounced if a proton-acceptor participates in the transition state, but this would almost certainly lead to a more complex relation between k and the solvent species than that found experimentally. Hammond (*J. Amer. Chem. Soc.*, 1955, **77**, 334), in a discussion of Melander's results for bromination and nitration has suggested that, although they show that the breaking of the C–H bond makes little progress in the attainment of the first transition state leading to the formation of the intermediate (II), they do not establish that the C–H bond is not broken in the rate-determining step of the reaction, since the removal of a proton from the intermediate (II) may require only a very slight weakening of the C–H bond to yield the second transition state preceding the formation of the products. The further observation is made that some loosening of the C–H bond might be expected in the formation of the intermediate in the change from the trigonal to the tetrahedral configuration of the nuclear carbon atom, although Melander (*loc. cit.*, p. 246) does not hold this view. It is probable that some stretching and bending of the C–H bond is more likely to occur in cyclodehydration than in nitration or bromination during the formation of a transition state (whether this leads to the intermediate or directly to the products) since the electrophilic attack of the side-chain is sterically hindered as a result of its attachment to the ring; a small isotope effect would then be the expected result.

Experimental

Preparation of 2-(2 : 4 : 6-Trideuteroanilino)pent-2-en-4-one.—2 : 4 : 6-Trideuteroaniline was prepared by Best and Wilson's method (*J.*, 1946, 2391). Aniline hydrochloride (13 g.) was heated with heavy water (20 g.) in a sealed tube in boiling water for 24 hr. This treatment was repeated five times, the water being removed by vacuum-distillation and replaced by a fresh sample each time. The first five treatments were carried out with heavy water containing 99·73 atoms % of deuterium and the last with a sample containing 99·95 atoms % of deuterium. The deuteroaniline was removed by making the residue alkaline and extracting it with ether. After removal of the ether, the liquid was distilled and the fraction boiling at 180° was collected. It was condensed with a slight excess of acetylacetone as described in Part I. Colourless crystals, m. p. 51—53°, of the *deutero-compound* were obtained from light petroleum (b. p. 40—60°). We are greatly indebted to Dr. R. I. Reed and Mr. A. Macdonald, of the University of Glasgow, for a mass-spectrographic examination of the water formed by combustion of this product (and of the quinoline compound obtained from it, referred to in the next paragraph). Their analysis gave 5·71 ± 0·02% D_2O by wt. from 0·0427 g. of the deuteroanilino-ketone diluted with 0·1416 g. of the protium-analogue (Calc.: 5·82% D_2O).

Test for Deuterium Exchange during Cyclodehydration.—The 6 : 8-dideutero-2 : 4-dimethylquinoline formed in the kinetic experiments in 95·7% sulphuric acid was separated by addition of sodium hydroxide and extracted with ether. The ether extract was washed with water, dried (Na_2SO_4), and filtered, and the ether was removed. Mass-spectrographic examination of the water obtained by combustion gave 4·68 ± 0·02% D_2O by wt. from 0·1060 g. of sample (Calc.: 4·78% D_2O). Deuterium exchange with the medium during the cyclodehydration was therefore not significant.

Kinetic Measurements.—The rates of cyclodehydration of the protio- and deutero-compounds in the two sulphuric acid media were measured by the method described in Part I.

We thank Professor Gwyn Williams for his interest in this work, the Central Research Fund for a grant for the purchase of heavy water, and this College for a postgraduate studentship (to J. M. W.).

Royal Holloway College (University of London),
Englefield Green, Surrey. [*Received, February 24th*, 1955.]

Lanthanon Sulphites and their Separation by Selective Oxidation.

By R. C. Vickery.

[Reprint Order No. 6076.]

Evidence is produced suggesting that under certain conditions lanthanon "bisulphite" solutions contain the anion $[Ln(SO_3)]^{3-}$. The preparation and properties of simple and complex lanthanon sulphites are described.

Oxidation of double sulphites to double sulphates has been employed as a means of separating the light from the heavy lanthanons. By fractional oxidation of the anionic trisulphito-complex to cationic sulphates, which are progressively removed by a cation-exchange resin, good separations are obtained within the light and the heavy lanthanon group.

The success achieved in separating the lanthanons by means of their complexes with polycarboxylic amino-acids has tended to overshadow the use of simpler compounds for this purpose; so it is appropriate to re-examine some of the longer-known, simpler reactions of the lanthanons and to assess their value for separation of lanthanons. The use of lanthanon sulphites as the starting point of a homogeneous double sulphate precipitation appeared attractive although there was little information available on their chemistry.

The simple lanthanon sulphites were first prepared by Berthier (*Ann. Chim. Phys.*, 1843, **7**, 74) and Marignac (*ibid.*, 1853, **38**, 167), and some of the alkali double sulphites were prepared and examined by Cuttica (*Gazzetta*, 1923, **53**, 769), but hitherto their only application to separations has been for the removal of thorium from lanthanon compounds (Chavastelon, *Compt. rend.*, 1900, **130**, 781; Bartek, *Z. anorg. Chem.*, 1905, **44**, 87; Grossman, *ibid*, p. 229). A more detailed study of these compounds was therefore

undertaken and two processes have been devised which provide effective means of separating the lanthanons.

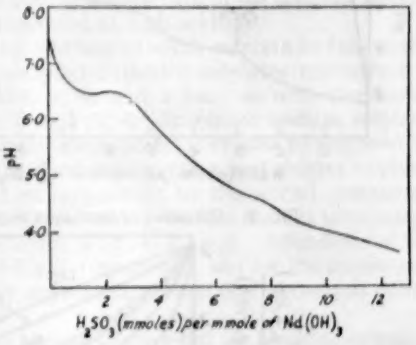
Lanthanon " Bisulphites."—On passage of sulphur dioxide through an aqueous slurry of lanthanon oxide, hydroxide, or carbonate, a solution is obtained in which the lanthanon has been assumed (Cuttica, *loc. cit.*) to be associated with the bisulphite ion as $Ln(HSO_3)_3$. On removal of part of the sulphur dioxide, by strongly heating the solution or reducing the pressure, lanthanon sulphite is precipitated, but can be redissolved by the further passage of sulphur dioxide. The reaction has been represented by Cuttica as the equilibrium :

$$2Ln(HSO_3)_3 \rightleftharpoons Ln_2(SO_3)_3 + 3SO_2 + 3H_2O$$

and this is supported by the titration curve for $Ln(OH)_3$ against H_2SO_3 (Fig. 1), which indicates the formation of a compound with a Ln : SO_3 ratio of 1 : 3. However, this is equally compatible with evidence now presented that under certain conditions the lanthanon is associated with SO_3^{2-} as a complex anion.

A spectrophotometric examination of neodymium " bisulphite " solutions showed effects similar to those previously observed in sequestered lanthanon compounds (Vickery, *J.*, 1952, 421). The 673 mμ absorption band of 0·1M-neodymium chloride was absent from 0·1M-neodymium " bisulphite." Bands at 510 and 475 mμ were unaffected but the 576, 522, and 463 mμ bands were displaced 12, 10, and 6 mμ respectively to longer wavelengths, with the 576 mμ band displaying six discrete peaks. The other bands showed similar evidence of dissection. These changes were most marked between the pH values 5·5 and 6·1. Over the pH range 5·5—3·5, neodymium sulphite was gradually precipitated, but it redissolved at pH 3·5, and the absorption spectrum assumed the form characteristic of ionic neodymium compounds; above pH 6·1, until the hydroxide was precipitated quantitatively at *ca.* pH 7·3, it was characteristic of the ionic form. Thus the spectroscopic evidence is consistent with the formation of a complex which is stable within pH range 5·5—6·1.

FIG. 1. *Titration of* $Nd(OH)_3$ *against* H_2SO_3.



In Fig. 2 a comparison is made of acid–base titrations of lanthanon chloride and lanthanon " bisulphite " solutions. The curve for the latter, unlike that for the chloride, shows points of inflexion corresponding to 3, 5, and possibly 7 equiv. of alkali. At pH 3·8, corresponding to 3 equiv. of alkali, a sodium salt was precipitated of composition $Na_3[Ln(SO_3)_3]$ in which the lanthanon has its usual covalency of six. This formula being assumed correct, subsequent steps in the titration could be considered as signifying progressive replacement of sulphite to form the basic salts $Na_3[Ln(SO_3)_2(OH)_2]$ and $Na_3[Ln(SO_3)(OH)_4]$ and finally $Ln(OH)_3$.

The evidence thus available is suggestive of the initial formation, not of bisulphite, but of the complex anion $[Ln(SO_3)_3]^{3-}$ and this should be readily detected by ion-exchange techniques. On using an anionic resin giving chloride ions on exchange, three chloride ion equivalents were found to be replaceable by one equivalent of lanthanon " bisulphite " solution (Table 1) :

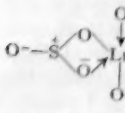
$$3Cl_{resin} + H_3[Ln(SO_3)_3] \longrightarrow Ln(SO_3)_{3\,resin} + 3HCl$$

TABLE 1. *Uptake of lanthanons by anion-exchange resins.*

[100 ml. of " bisulphite " solution equiv. to 1 g. of $Ln(OH)_3$ equilibrated with 25 g. of Deacidite FF.]

pH	Ln	Uptake (%)	Cl^- in eluate (g.)	Ratio, $Cl_{eluted}/Ln_{abs.}$	pH	Ln	Uptake (%)	Cl^- in eluate (g.)	Ratio, $Cl_{eluted}/Ln_{abs.}$
5·3	La	100	0·458	2·92	6·2	La	99·9	0·420	3·03
	Yb	100	0·515	3·07		Nd	100	0·600	3·20
5·6	La	100	0·425	3·06		Yb	99·9	0·505	3·14
6·0	Nd	99·8	0·590	3·11					

The possible presence in the " bisulphite " solution of such compounds as $H_2[Ln(SO_3)_3]^-$ and $H[Ln(SO_3)_3]^{2-}$ cannot be disregarded, but the constancy of the exchange value between the critical pH values supports the view that the lanthanon trisulphito-ion, $[Ln(SO_3)_3]^{3-}$, is the main component of lanthanon " bisulphite " solutions. A possible configuration of this ion would consist of three four-membered chelate rings (see inset), and such a weakly chelated structure could account for the spectroscopic observations and for the lability of the ion under the influence of heat or reduced pressure.



Oxidation of Lanthanon Trisulphito-complex.—Solutions of these lanthanon compounds are readily oxidised by air or oxygen to the sulphates (Fig. 3). The rate of oxidation of the yttrium solution occupies an anomalous position between those of neodymium and

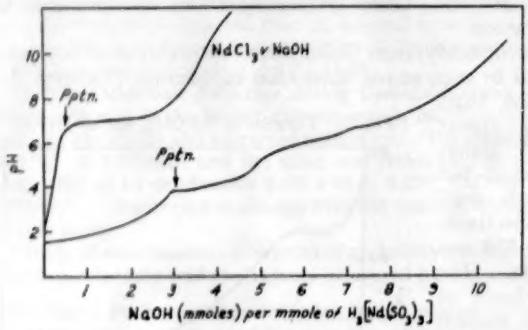
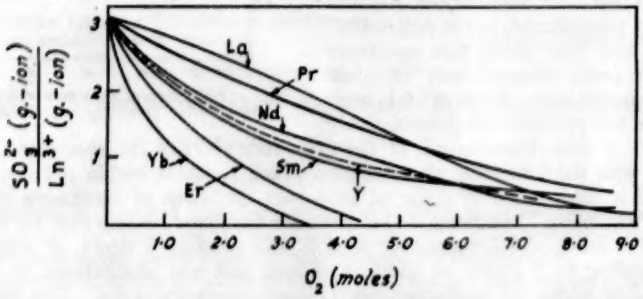


FIG. 2. *Titration of* $H_3[Nd(SO_3)_3]$ *against* NaOH.

FIG. 3. *Oxidation of lanthanon trisulphito-complexes in* 0·1M*-solution at* 20°.



samarium. This is out of conformity with the serial order of simple ionic size, but is consistent with the formation of complex compounds (Marsh, *J.*, 1947, 1084; 1951, 1337, 1461; Vickery: " Chemistry of the Lanthanons," Butterworths, London, 1953). Unlike the lanthanon complexes previously studied, however, the stability of the trisulphito-complex decreases with increase in atomic number of the lanthanon. It is evident from the oxidation curves that, under the conditions of these experiments, oxidation to sulphates occurs without the intermediate formation of sulphites. For example, there is no inflexion in the oxidation curve for the yttrium compound suggesting a change from the covalent to the ionic form which would place it in its normal serial position near holmium. Further, lanthanon sulphites are only sparingly soluble and if formed would have been precipitated. Whether or not this oxidation is a chain reaction cannot be deduced from the evidence available but the overall reaction may be represented by

$$4H_3[Ln(SO_3)_3] + 3O_2 \longrightarrow 2Ln_2(SO_4)_3 + 6SO_2 + 6H_2O$$

Lanthanon Sulphites.—These may be prepared from solution of the trisulphito-complexes by partial removal of sulphur dioxide by heat or reduced pressure. Sulphites of

the heavy lanthanons are readily precipitated at 45°, but those of the light lanthanons not below 70°. This difference in temperature suggested a means of separation but attempts to apply it were unsuccessful because of occlusion of light lanthanons in the heavy lanthanon sulphite precipitate even when the temperature was kept at 50°. Whether precipitated by reducing the pressure or by heating, the sulphites are microcrystalline, but their habit could not be defined microscopically. By either method of precipitation they formed hydrates as follows:

Lanthanon	La	Ce	Pr	Nd	Sm	Gd	Dy	Er	Yb	Y
Water of crystn. (moles)	4	5	5	4	3	8	8	8	8	4

Lanthanon sulphites are sparingly soluble in water at 20°, the solubilities ranging from *ca.* 0·2 g./l. for the lanthanum to 0·6 g./l. for the ytterbium salt. They are decomposed by mineral acids and aqueous oxalic acid with evolution of sulphur dioxide. By passage of this gas through aqueous suspensions of the sulphites they are readily dissolved but they are not converted into carbonate or otherwise affected by passage of carbon dioxide. They dissolve in ammonium acetate solutions and are not reprecipitated from these solutions by addition of acid (cf. acetatosulphate complexes; Vickery, *J.*, 1950, 1101). This should not, however, be interpreted as indicating the strength of the complex formed, for doubtless the sulphites are completely decomposed at high acidities.

Double Sulphites.—As normally prepared by addition of alkali sulphite to hot, nearly neutral lanthanon chloride solutions, the precipitated double sulphites correspond to the formula $xLn_2(SO_3)_3.yR_2SO_3.zH_2O$, in which x, y, and z vary as with the double sulphates but are normally in the ratio 1 : 1 : 2 or 1 : 1 : 4. In cerium sodium sulphite, however, the ratio is commonly 1 : 2 : 4. The double sulphites may also be prepared by heating or evacuating a solution containing the trisulphito-complex and sodium sulphite. Double sulphites prepared by the first method are crystalline; by the second, gelatinous. They are slightly soluble in water, values at 20° for the crystalline sodium salts being: for lanthanum (1 : 1 : 2) 0·4 g./l. and for ytterbrium (1 : 1 : 4) 3·3 g./l. Solubilities of the corresponding potassium salts were 1·4 and 5·3 g./l. respectively, and for the ammonium salts 2·2 and 10·4 g./l. These values are only approximate, since slow hydrolysis occurs when these compounds are suspended in water.

The double sulphites dissolve in ammonium acetate solution but the resulting complex, in contrast to the analogous complexes formed by the double sulphates, does not yield a precipitate on addition of acid. Metathesis of the solid double sulphites to hydroxide or oxalate is readily accomplished.

Separation of Lanthanons by Homogeneous Double Sulphate Precipitation.—Double sulphates are precipitated by oxidation of the solution obtained by adding sulphite to an acid solution of lanthanon chloride. Oxidation may be effected by air, oxygen, or hydrogen peroxide and catalysed by the additions of such ions as Cu^{2+}, Mn^{2+}, and Fe^{2+}. This reaction was investigated as an improved technique of double sulphate separation and it was found that, although oxidation by air or oxygen was easy to control, yet the use of hydrogen peroxide or catalysts gave unduly high rates of oxidation and made fractionation difficult.

The pH range through which this reaction can be effected is quite narrow. Provided the pH of the mixture be kept between 1·3 and 2·0 by addition of hydrochloric acid, M-sodium sulphite solution (pH 9·4) can be added to M-lanthanon chloride solution without evolution of sulphur dioxide or precipitation of lanthanons. Below pH 1·3, satisfactory oxidation of sulphite has not been obtained; above pH 2·0 lanthanon double sulphites are precipitated. Since it is desirable to work in a solution containing as little acid as possible, a pH range of 1·6—1·8 was adhered to,* and to ensure precipitation of heavy lanthanon double sulphates, sodium chloride was added to the solution (Marsh, *Nature*, 1949, **163**, 998).

* At this acid level the formation of HSO_3^- rather than SO_3^{2-} ions might be expected. However, the addition of sodium hydrogen sulphite solution to one of lanthanon chloride effected precipitation at pH 1·7, and even when the pH was kept at 1·3—1·5 oxygenation produced no precipitate of lanthanon double sulphate—possibly under these conditions bisulphite ions are oxidised directly to bisulphate which would not precipitate the lanthanons.

In separations based on this homogeneous double sulphate precipitation, two aspects were examined: a comparison of the conventional double sulphate separation of the light and heavy lanthanon groups, and the effectiveness of separating individual members. The separations achieved are shown in Table 2. An enhanced degree of separation of

TABLE 2. *Lanthanon separation by double sulphate fractionation.*

Fractionation of 150 g. of oxide of original composition: Pr, 8; Nd, 35; Sm, 8; Gd, 5; Dy, 2; Er, 10; Yb, 12 (as Ln_2O_3) %.

	Homogeneous pptn. Ln_2O_3 (%)								Heterogeneous pptn. Ln_2O_3 (%)							
No.	Wt. (g.)	Pr	Nd	Sm †	Gd	Dy	Er	Yb	Wt. (g.)	Pr	Nd	Sm †	Gd	Dy	Er	Yb
1	17·2	9·9	32	—	—	—	—	—	15·9	12·5	39·3	—	—	—	—	—
2	22·3	16·2	70·9	—	—	—	—	—	17·3	17·9	55·0	0·6	—	—	—	—
3	22·3	17·1	73·1	0·9	—	—	—	—	19·2	18·3	64·5	2·1	—	—	—	—
4	15·2	12·5	62·5	21·0	1·2	—	—	—	15·5	13·3	76·5	7·7	1·3	0·6	—	—
5	10·0	8·0	38·0	51·0	20·0	1·0	—	—	12·5	8·0	60·0	23·0	1·5	0·8	4	2·4
6	8·6	2·3	17·0	25·5	30·2	1·1	23·2	—	13·4	2·2	23·0	27·6	19·3	2·2	11·2	6·7
7	7·6	—	2·6	5·2	30·2	5·3	40·5	15·8	14·9	0·7	8·0	18·1	15·4	5·4	19·4	16·1
8	12·6	—	—	2·4	15·1	7·1	27·8	23·8	16·1	—	1·8	5·6	11·8	6·8	23·0	23·6
9	14·3	—	—	—	0·7	7·0	22·3	22·3	11·9	—	—	4·4	8·4	3·4	32·0	33·6
10	9·6	—	—	—	—	1·0	18·0	49·0	8·4	—	—	—	—	2·0	23·0	45·7
11	6·0	—	—	—	—	1·6	8·3	50·2	5·1	—	—	—	—	1·9	11·7	56·7
12*	2·5	—	—	—	—	—	12·0	84·1	3·1	—	—	—	—	2·0	10·0	67·8

* Final oxalate precipitate. † Probably high, owing to the presence of Fe^{3+}.

light from heavy lanthanons is evident, but within the lighter group separations were confined to a good concentration of samarium in the tail fractions. In the middle lanthanon fractions good concentrations of gadolinium and dysprosium were obtained. In view of the relatively high concentrations of erbium and ytterbium in the initial material their accumulation is not noteworthy. In general, fractionation by this homogeneous method is most effective in separating the middle lanthanons, samarium to dysprosium, and thus also in giving enhanced separations of both light and heavy lanthanons.

Separation of Lanthanons by Anion–Cation Conversion of Trisulphito-complexes.—In addition to the homogeneous conversion of lanthanon double sulphites into double sulphates, a further method has been devised based on the different rates of oxidation of the anionic complexes $[Ln(SO_3)_3]^{3-}$ to the corresponding sulphates (Fig. 3). (This process is part of the subject matter of Australian Patent Appln. 14,772/52.)

Fractionation was effected by a succession of partial oxidations followed at each stage by adsorption of the sulphates on a cation-exchange resin. The sulphates were subsequently stripped from the resin by a solution of sodium ethylenediaminetetra-acetate, and the resin regenerated by sodium chloride. Oxidation was effected by molecular oxygen with the solution buffered to pH 5—7. The heavy lanthanons separated first, and the results given in Table 3 indicate an excellent concentration of ytterbium and appreciable

TABLE 3. *Separation of heavy lanthanons by anion–cation conversion.*

	Dy	Er	Yb		Dy	Er	Yb
Original	6	18	20		—	—	—
Fraction 1	—	6	62	Fraction 5	15	57	10
„ 2	—	18	60	„ 6	26	41	—
„ 3	3	25	51	„ 7	24	27	—
„ 4	9	39	31	„ 8	18	10	—

separation of dysprosium and erbium. The lighter lanthanons are also extracted in the order of decreasing atomic numbers (Table 4). Good concentrations of samarium were obtained, and praseodymium was concentrated with residual lanthanum towards the tail fractions with some separations from neodymium.

Separations of the lanthanons by this technique do not compare, in purity of product, with those obtained by conventional ion-exchange techniques. On the other hand, this new technique is not limited by the capacity of the resin to effect this conversion; the resin

TABLE 4. *Separation of light lanthanons by anion–cation conversion.*

	Pr	Nd	Sm		Pr	Nd	Sm
Original	10	50	15	Fraction 6	12	79	9
Fraction 1	—	10	52	,, 7	15	82	2
,, 2	—	18	48	,, 8	28	63	—
,, 3	2	26	50	,, 9	40	58	—
,, 4	—	42	31	,, 10	48	38	—
,, 5	10	66	16	,, 11	52	30	—

functions solely as a collector of sulphate already produced. This method has the advantage that larger quantities of lanthanons can be handled with greater facility, yielding concentrates which, after second or third fractionations, are of a quality comparable with those obtained by other methods.

EXPERIMENTAL

Materials and Analytical Methods.—Lanthanon hydroxides used in the preparative work were of >98% purity. The neodymium oxide was of "Specpure" quality. The lanthanon mixtures were prepared from various sources: the light lanthanons were obtained chiefly from monazite, some cerium and lanthanum having been removed; the heavy lanthanons were extracted from South Australian davidite, and freed from much yttrium. Sulphur dioxide, oxygen, and nitrogen were of commercial quality. The anion-exchange resin was Deacidite FF in the chloride form, and the cation-exchange resin was Dowex-50 in the sodium form.

Spectrophotometric measurements were made with the Unicam and the Beckman D.U. instruments, and electrometric titrations were followed on a Cambridge pH meter. Lanthanons were determined as oxide after ignition of the oxalates, and sulphite was determined iodometrically. The degree of hydration of the simple and double sulphites was determined by drying first in a vacuum-desiccator (conc. H_2SO_4) and then in an air-oven at 110°. During this treatment insignificant oxidation of the solid sulphites occurred; even after 24 hours' exposure to the atmosphere in an open dish, solid neodymium sulphite contained only 1·1% of SO_4^{2-}. Solubilities were roughly determined by shaking an excess of the salt with distilled water for 24 hr., filtering the suspension, and evaporating an aliquot part of the filtrate to dryness in platinum under an infrared lamp.

The *neodymium salt* obtained at pH 3·8 by titrating the solution containing the trisulphito-complex with sodium hydroxide (Fig. 2) was microcrystalline and anhydrous. Sulphite was determined iodometrically, lanthanons as oxalates, and sodium as the zinc uranyl acetate salt [Found: SO_3, 52·8; Ln_2O_3, 37·2; Na, 14·9. $Na_3Ln(SO_3)_3$ requires SO_3, 53·2; Ln_2O_3, 36·8; Na, 15·4].

The charges on the trisulphito-complex were determined by shaking 25 g. of Deacidite FF resin with 100 ml. of a solution of the complex containing the equivalent of 1 g. of Ln_2O_3 for 24 hr. in an atmosphere of nitrogen. Equilibrium was assumed to have been reached after this period, and the resin was filtered off, and, from the combined filtrate and washings, lanthanons were precipitated as oxalates, and chloride as silver chloride (Table 2).

Oxidation rates were determined by use of the apparatus shown in Fig. 4. Sulphur dioxide was passed at 20 ml./sec. through 250 ml. of a 0·1M-slurry of lanthanon hydroxide in the central reaction cell for 3 min., by which time all lanthanons had dissolved. After passage of nitrogen through the solution at 30 ml./sec. for 30 min. to remove excess of sulphur dioxide, the sulphite content of the solution was determined iodometrically. Oxygen was then passed through the solution at 20 ml./sec., and 2 ml. samples were collected and titrated in an atmosphere of nitrogen first at 3-min. intervals but at longer intervals as oxidation progressed. In calculating the results shown in Fig. 3 corrections were made for the samples removed. The temperature was maintained at 20° ± 1·5° by circulating water through the jacket of the cell.

Separation of Lanthanons by Homogeneous Double Sulphate Precipitation.—Hydrochloric acid was added to 1500 ml. of 10% $LnCl_3$ solutions to reduce the pH to 1·4. Sufficient sodium sulphite was added to produce later a suitable amount of double sulphate without increasing the pH above 1·8: 30 g. of $Na_2SO_3.7H_2O$ generally yielded 8—10 g. of double sulphate, and up to 60 g. of the anhydrous sulphite could be added before pH adjustment with acid was necessary; the pH was finally adjusted to 1·6—1·8 by addition of sodium sulphite or hydrochloric acid and the solution was heated to 80° whereat oxygen was passed through the solution at 20 ml./sec. until precipitation reached sufficient proportions. After the precipitate had been filtered off oxygen was again passed through the filtrate, further sodium sulphite being added if necessary, and the sequence of filtration and further oxygenation repeated.

In Table 2, the efficiency of double sulphate fractionation by this homogeneous method is compared with that obtained by the normal heterogeneous procedure. The latter was carried out by the simple intermittent addition of anhydrous sodium sulphate to 10% $LnCl_3$ solution at 80—90° and pH 2·5, the solution being saturated with sodium chloride and well stirred. Double sulphate fractions obtained by either mode of precipitation were converted into hydroxides, washed free from alkali, ignited to oxide, and analysed spectrophotometrically by using the extinction coefficients and wavelength data given by Moeller and Brantley (*Analyt. Chem.*, 1950, **22**, 433) and Wylie (*J. Soc. Chem. Ind.*, 1950, **69**, 143). Analyses for gadolinium are subject to the ±10% error noted by Moeller and Brantley but other values have been appropriately corrected for interfering ions.

Separation by Anion–Cation Conversion.—This separation can be carried out as either a batch, or a cyclic process, but the former is less satisfactory because of the necessity of handling

FIG. 4. *Apparatus for measuring rate of oxidation.*

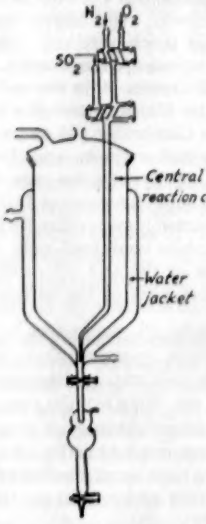
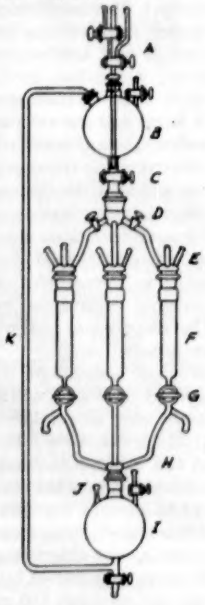


FIG. 5. *Apparatus for separation of lanthanons by oxidative anion–cation conversion.*



a large bulk of liquid in an inert atmosphere. All results recorded here were obtained by a cyclic process conducted in the equipment shown in Fig. 5. A slurry of lanthanon hydroxides contained in the main reaction vessel *B* was dissolved by sulphur dioxide admitted through one branch of the triple manifold *A*. After dissolution, nitrogen was passed through another branch of the manifold to displace the excess of sulphur dioxide before introduction of oxygen through the third branch of the manifold. Oxygenation having proceeded for an appropriate time, nitrogen was again introduced to give an inert atmosphere, whilst the partially oxidised solution was led *via* the main tap *C* and the distribution head *D* into one of the "collector" columns F. The ground-in adaptors to these columns, *E*, carried three additional inlets for wash-water, sodium "enta" stripping solution, and brine regenerant solution.

After passing through the columns, the unoxidised solution was directed by the two-way tap *G* to the collector head *H* and thence to the receiving vessel *I*. When finally collected in *I*, the solution and washings from the columns were blown by nitrogen pressure *via J* up the return line *K* to the main reaction vessel *A* for further oxygenation. During this return of the solution to *A* and further oxidation, the collector column was being stripped of its adsorbed lanthanons by 5% sodium "enta" solution at pH 8—8·5, washed free from excess of stripping solution,

regenerated with sodium chloride solution, and then washed free from excess of chloride. All these solutions were directed from the columns by the tap *G* to an external receiver. These treatments of the collector column invariably required more time than was required for return of the lanthanon solution to *A* and its further oxidation, so it was necessary to direct the re-oxidised lanthanon solution to a second column for extraction of the second fraction of lanthanon sulphate. In practice six collector columns were operated in rotation.

Sulphur dioxide, nitrogen, and oxygen were measured through flow-rate manometers, and the stripping and regenerant solutions were dispensed from aspirators on a shelf 18" above the main reaction vessel. The whole assembly was erected inside a steel framework of supporting bars and platforms at the appropriate levels.

The selectivity of the anion–cation conversion is related to the dilution of the lanthanon solution; for maximum efficiency the concentration of the solution should be between 0·5 and 6·0% and preferably between 3 and 4%. Below 0·5% the complex undergoes some hydrolysis.

To ensure complete removal of cation from solution, an excess of exchange resin must be used; this can be determined from the capacity of the resin, the oxidation curves, and the duration of oxidation. The resin must be used in the sodium form; a hydrogen resin would, on exchange, depress the pH of the solution to below that at which the complexes are stable. Time of contact between solution and resin is also of importance.

In a typical run the operating conditions were: sulphur dioxide at 50 ml./min. was passed through 4 l. of hydroxide slurry containing 140 g. of $Ln(OH)_3$. On completion of solution, nitrogen was passed at 30 ml./min. for 2 min. and then oxygen at 20 ml./min. for 20 min. to give a maximum yield of 8 g. of Ln^{3+}. After this oxygenation, nitrogen was again passed for 2 min. and the solution was then passed through the exchange column, containing 250 g. of resin, at 1500 ml./hr. After the column had been washed with 100 ml. of water the lanthanon solution plus washing was blown back to the reaction vessel for further oxygenation. The resin column was stripped by the slow (5 ml./min.) passage of the stripping solution, washed with 500 ml. of water, and then regenerated by the slow passage of 2 l. of 2% sodium chloride solution, again followed by washing. The lanthanons contained in the stripped fraction were recovered by precipitation as oxalate after acidification of the solution to pH 3.

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Superoxide Ions in Commercial Sodium Peroxide.

By PHILIP GEORGE.

[Reprint Order No. 6088.]

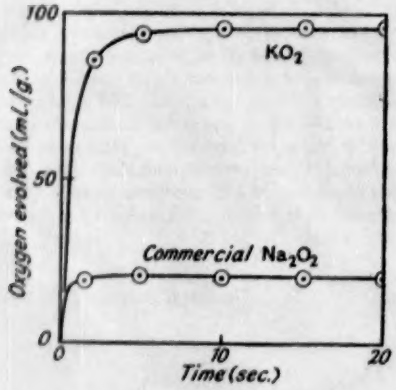
Experiments on the pale yellow sodium peroxide available commercially show it to contain about 10% of sodium superoxide, the sodium salt of the HO_2 free radical. In water, oxygen is evolved extremely rapidly according to the scheme $2NaO_2 + 2H_2O \longrightarrow O_2 + H_2O_2 + 2NaOH$, analogous to the very rapid evolution given by the deep orange paramagnetic potassium superoxide. Two different samples of the pale yellow sodium peroxide were paramagnetic, with $\chi = 2{\cdot}7$ and $2{\cdot}2 \times 10^{-6}$ c.g.s. units. These values correspond to the presence of 9·2% and 7·7% of NaO_2 respectively. A determination of the sodium content of the former sample confirmed this.

ALTHOUGH potassium, rubidium, and cæsium form two higher oxides, the peroxides and the superoxides containing the ions $O_2^{=}$ and O_2^{-} respectively, it was long thought that sodium could form only the peroxide (Holt and Sims, *J.*, 1894, **65**, 432; Rengade, *Ann. Chim. Phys.*, 1907, **11**, 348; Kraus and Whyte, *J. Amer. Chem. Soc.*, 1926, **48**, 1781; Neuman, *J. Chem. Phys.*, 1934, **2**, 31). Joannis (*Compt. rend.*, 1893, **116**, 1870) claimed that an oxide corresponding to Na_2O_3 was formed by oxidising sodium in liquid ammonia at −50°, although Kraus and Whyte found that only the peroxide was formed at −33°.

George (*Discuss. Faraday Soc.*, 1947, **2**, 203, 218) reported that pale yellow samples of commercial sodium peroxide contain about 10% of NaO_2, and Schechter, Sisler, and

Kleinberg (*J. Amer. Chem. Soc.*, **1948**, **70**, 267) reported that NaO_2 is present in solutions of sodium treated with oxygen in liquid ammonia at −77°. These investigations, the first based on paramagnetic-susceptibility determinations, measurements of oxygen evolution, and sodium analyses, and the second on oxygen-absorption measurements, first established that sodium forms the superoxide as do the heavier alkali metals. Schechter, Thomson, and Kleinberg later (*ibid.*, **1949**, **71**, **1816**) showed that under optimum conditions up to 85% of NaO_2 can be prepared in liquid ammonia; Stephanou, Schechter, Argersinger, and Kleinberg (*ibid.*, p. 1819) obtained yields of NaO_2 as high as 92% by treating Na_2O_2 with oxygen at 490°/298 atm.; and Seyb and Kleinberg (*Analyt. Chem.*, **1951**, **23**, 115) described an oxygen-evolution method for estimating NaO_2 and the amount present in synthetic NaO_2–Na_2O_2 mixtures.

The experiments on the commercial sodium peroxide have not hitherto been reported in detail because many of the essential features are covered by the work of Kleinberg *et al.* The present publication was decided upon for two reasons. The commercial Na_2O_2 containing about 10% of NaO_2 provides a useful magnetically dilute material for studying the paramagnetic resonance absorption of the O_2^- radical (Bennett, Ingram, Symons, George, and Stanley Griffith, *Phil. Mag.*, **1955**, **46**, 443), and it is therefore desirable to substantiate fully the presence of O_2^- by physical and chemical means. Secondly, it is desirable to draw attention to the fact that such a readily available material contains the O_2^- ion, and that for many experiments on O_2^- the commercial sodium peroxide may be used in place of NaO_2, KO_2, etc., which are somewhat difficult to prepare.



A comparison of the oxygen evolution when a sample of potassium superoxide containing 61% of KO_2, and sodium peroxide, react with water, showing the small but equally rapid evolution from sodium peroxide attributable to the presence of 10·3% of NaO_2.

Results.—There is both qualitative and quantitative evidence for the existence of superoxide ions in certain commercial samples of sodium peroxide.* The qualitative observation that many samples are pale yellow is clearly at variance with a composition $[2Na^+, O_2^=]$. The colour has occasionally been attributed to traces of iron, but the samples examined contained only 0·017%, which makes this explanation extremely unlikely. Superoxides are deep orange at room temperature, so the presence of some 10% of superoxide ions in the samples of sodium peroxide is in accord with their pale yellow colour. The quantitative evidence is based on measurements of oxygen evolution, paramagnetic susceptibility, and sodium content.

Oxygen evolution. It is well known that superoxides evolve oxygen extremely rapidly in water according to reaction (1). George (*loc. cit.*) suggested that the most probable mechanism is proton transfer (2), followed by rapid electron transfer (3). Samples of sodium peroxide (20—30 mg.) also evolve a small amount of oxygen extremely rapidly,

* A sample of sodium peroxide used in America was quite white and presumably contained no O_2^-, whereas most samples available in this country are pale yellow like those used in these experiments. Apparently the conditions used in the industrial preparation are sufficiently dissimilar to favour a different equilibrium mixture in the reaction $O_2^= + O_2 \rightleftharpoons 2O_2^-$.

as shown by the comparison with KO_2 in the Figure: in both cases the evolution is complete in less than 3 sec. The results are given in terms of oxygen evolved per g. at N.T.P., and the figure for sodium peroxide, 21 ml./g., corresponds to 10·3% of NaO_2 present.

$$2KO_2 + 2H_2O \longrightarrow O_2 + H_2O_2 + 2KOH \quad . . . . . (1)$$

$$2O_2^- + H_2O \longrightarrow O_2^-{\cdot}O_2H + OH^- \quad . . . . . (2)$$

$$O_2^-{\cdot}O_2H \longrightarrow O_2 + O_2H^- \quad . . . . . (3)$$

Oxygen is evolved from the hydrogen peroxide liberated by the solution of the Na_2O_2 and the decomposition of the NaO_2 far more slowly, at least an hour being required for complete reaction. The rate of the initial rapid evolution is greater than 20 ml. $g.^{-1}$ $sec.^{-1}$, compared with 0·03 in the subsequent peroxide decomposition, so the rates thus differ by a factor of at least 600. However, if a catalyst is present, then a large proportion of the peroxide is also decomposed in 3—5 sec. With 1·0M-Fe^{3+}, 74% and 46% of decomposition was obtained in water and in 5·0N-sulphuric acid respectively: and with 1·0M-Fe^{2+}, 63% and 44%. Acidic saturated solutions of sodium persulphate gave 16%, but with 0·1M-Ag^+ ions present, and in alkaline solution, 87% and 80% decomposition was observed. These results are very similar to those obtained with KO_2 (George, *loc. cit.*), and confirm that this rapid catalytic decomposition, like the reaction of the O_2^- ions, occurs predominantly within the environment of the solid peroxide or superoxide particles as they dissolve, with however, some of the hydrogen peroxide diffusing away, for otherwise 100% decomposition would be obtained.

Paramagnetic susceptibility. Superoxides are paramagnetic, for they contain the ion-radical O_2^-, an oxygen molecule with an additional electron (Neuman, *J. Chem. Phys.*, 1934, **2**, 31). The susceptibility of two samples of sodium peroxide has been measured, and in both cases they were paramagnetic with mass susceptibilities of $\chi = 2{\cdot}7$ and $2{\cdot}2 \times 10^{-6}$ c.g.s. units. By extrapolation from the value for 92% NaO_2, Stephanou, Schechter, Argersinger, and Kleinberg (*loc. cit.*) obtained $\chi = 33{\cdot}0 \times 10^{-6}$ c.g.s. units for the pure compound. This value is uncorrected for the diamagnetic contribution, which, although affecting the value for the pure compound only slightly, will be increasingly important as the percentage of NaO_2 in a mixture decreases. Savithri and Rao (*Proc. Indian Acad. Sci.*, 1942, **16**, *A*, 221) determined the molar susceptibility of Na_2O_2 as $\chi_M = -28{\cdot}1 \times 10^{-6}$ c.g.s. units, from which the susceptibility per g. can be calculated as $\chi = -0{\cdot}36 \times 10^{-6}$ c.g.s. unit. The susceptibilities of the two commercial sodium peroxide samples thus correspond to mixtures containing 9·2 and 7·7% of NaO_2 respectively.

The paramagnetism is a feature of the solid peroxide, because the syrupy liquid, obtained by cautiously adding the minimum amount of water dropwise to get the solid into solution, was found to be diamagnetic, with $k = -0{\cdot}5 \times 10^{-6}$ c.g.s. unit, and furthermore completely colourless. These observations show that the colour and the paramagnetism cannot be due to heavy-metal impurities, for, whilst solution might diminish the colour, the paramagnetism would remain.

Analysis. The sodium content of sodium peroxide provides a sensitive check on its composition. As well as Na_2O_2 (Na, 59·0%) and NaO_2 (Na, 41·8%), it may contain Na_2O (Na, 74·3%) produced by prolonged heating during the combustion, and also sodium carbonate (Na, 43·4%) resulting from reaction with carbon dioxide. The presence of Na_2O thus leads to a high value for the sodium content, and the presence of NaO_2 or Na_2CO_3 to low values. Both samples of commercial sodium peroxide examined were fine, freely running powders, so the absorption of water vapour which would give hydrogen peroxide and sodium hydroxide, and hence a sticky solid, may be ignored.

The carbonate content of one of the samples was determined by the difference between the gas evolved from 0·1N-sulphuric acid and from 0·1N-sodium hydroxide, an independent check, involving absorption with potassium hydroxide, having shown that carbon dioxide as well as oxygen was evolved in acid solution. The mean of duplicate measurements gave a carbonate content of $9{\cdot}0 \pm 1{\cdot}3$%. Estimation of the sodium as anhydrous sulphate gave values of 55·6% and 55·8% in duplicate determinations. The mean sodium content of 55·7% is significantly below that for Na_2O_2 containing $9{\cdot}0 \pm 1{\cdot}3$% of Na_2CO_3 (*i.e.*,

57·5—57·8% Na), and, if it is assumed that the discrepancy is entirely due to the presence of NaO_2, calculation shows that 55·7% of Na corresponds to an NaO_2 content of 11%. This value is to be compared with those of 10·3% and 9·2% obtained from the oxygen evolution and the paramagnetic-susceptibility measurements on the same sample. The presence of Na_2O and the absorption of water vapour, which would also affect the sodium content, could not be estimated, but the very close agreement between the three determinations of superoxide ion content, which is well within experimental error, strongly suggests that these factors are negligible.

Although it seemed very unlikely, the possibility that the superoxide content of the commercial sodium peroxide was due to the presence of potassium needed checking. Tests with sodium cobaltinitrite showed that there was less than 1 part of potassium in 600 parts, far too little to account for a superoxide content of about 10%.

The main reason why the presence of the higher oxide has been overlooked for so long is probably that the purity of sodium peroxide is usually determined by estimating the hydrogen peroxide liberated on the addition of water. However, hydrogen peroxide is also formed from NaO_2, and so the Na_2O_2 content does not appear so low as it otherwise would. In fact, if estimated by peroxide titration, samples containing 10, 20, 30% of NaO_2 would still appear to be 97·2, 94·5, and 91·5% of Na_2O_2.

Experimental

Analysis for Iron.—Sodium peroxide (0·100 g.) was dissolved in water, neutralised with sulphuric acid, and evaporated to dryness to remove hydrogen peroxide. The residue was taken up in acetate buffer of pH 5·0, a little ascorbic acid added to reduce ferric to ferrous iron, and this was then estimated colorimetrically with 2 : 2′-dipyridyl. The 0·100 g. sample thus treated and made up to 100 ml.; the solution was found to contain 3×10^{-6}M-Fe^{2+}, corresponding to an initial content of 0·017% by weight.

Analysis for Sodium and Potassium.—This was carried out by treating a known weight of the peroxide with water, evaporating to dryness, adding an excess of concentrated sulphuric acid, again evaporating, heating to red heat, cooling, and weighing the anhydrous sodium sulphate formed: 0·4846 g. and 0·5255 g. of peroxide gave 0·7970 g. and 0·9047 g. of sulphate respectively. The sodium content of the peroxide is thus 55·6 and 55·8%; mean, 55·7%. Tests with sodium cobaltinitrite solution and a very dilute potassium chloride solution as a standard showed the potassium content of the peroxide to be less than 4 parts in 2500.

Oxygen Evolution.—The apparatus and method of operation were as described before (George, *loc. cit.*).

Magnetic Susceptibility.—This was measured at 19° by using a simple Gouy balance with a permanent magnet of field strength 4900 gauss and a cylindrical specimen tube of cross-sectional area 0·183 sq. cm. holding 1·4 ml. The solid peroxide samples showed a net increase in weight in the magnetic field of 6·1 and 7·4 mg., indicating paramagnetism, whereas their very concentrated solutions showed a decrease of about 1·1 mg., indicating diamagnetism. The balance was calibrated with a standard nickel chloride solution: 1 mg. $\equiv 0{\cdot}445 \times 10^{-6}$ unit of k, the volume susceptibility. The density of the packed samples was 1·25; hence the two samples had volume susceptibilities $k = 3{\cdot}3$ and $2{\cdot}7 \times 10^{-6}$, and mass susceptibilities $\chi = 2{\cdot}7$ and $2{\cdot}2 \times 10^{-6}$.

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Intramolecular Interaction between γ-Tertiary Amino- and Cyano-groups.

By M. W. Gittos and Walter Wilson.

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γ-Benzylmethylamino- and γ-dibenzylamino-αα-diphenylalkyl cyanides readily lose one benzyl group (as benzyl chloride) in hot hydrochloric acid, yielding 2-iminopyrrolidines. Analogous cyanides having one or two α-hydrogen atoms are hydrolysed normally under similar conditions, with only slight debenzylation. *γ-tert.*-Benzylamino-acid hydrochlorides are readily cyclised in hot acetic anhydride to pyrrolid-2-ones, benzyl chloride and acetate being formed simultaneously. Benzylamine and 3-chloropropyl cyanide react rapidly, to give ammonia and 1-benzyl-2-benzyliminopyrrolidine. Alkaline hydrolysis of the latter affords *N*-benzyl-γ-benzylaminobutyramide, which is synthesised by an independent method.

2-Iminopyrrolidines are readily obtained, along with benzyl chloride, by the action of boiling aqueous hydrochloric acid on γ-benzylmethylamino-αα-diphenylalkyl cyanides, *e.g.*, (I; R = R′ = Ph, R″ = Me) (Wilson, *J.*, 1952, 3524). This reaction probably involves an initial direct intramolecular interaction between the *tert.*-amino- and the cyano-group : $\geqslant N \curvearrowright C \equiv N \curvearrowright H^+$ (cf. Wilson, *Chem. and Ind.*, 1955, 200).

It has now been found that 3-dibenzylamino-1 : 1-diphenylpropyl cyanide (I; R = R′ = Ph, R″ = CH_2Ph) in boiling hydrochloric acid, or more quickly in acetic–hydrochloric acid, affords benzyl chloride and 1-benzyl-2-imino-3 : 3-diphenylpyrrolidine (II; R = R′ = Ph, R″ = CH_2Ph), the second benzyl group being stable. The structure of the iminopyrrolidine was confirmed by the formation of a basic *N*-acetyl derivative, and of a rather insoluble nitrate (cf. amidines; Walker, *J.*, 1949, 2000); nitrous acid also converted it into 1-benzyl-3 : 3-diphenylpyrrolid-2-one (III; R = R′ = Ph, R″ = CH_2Ph).

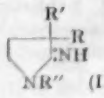
(I) NC·CRR′·CH_2·CH_2·NR″·CH_2Ph HO$_2$C·CHR·CH_2·CH_2·NR″R‴ (HCl) (IV)

3-Benzylmethylamino- and 3-dibenzylamino-1-phenylpropyl cyanide were obtained by aminoalkylating benzyl cyanide. These basic cyanides did not afford much benzyl chloride in aqueous hydrochloric acid, being mainly hydrolysed to the corresponding γ-dialkylamino-α-phenylbutyric acids (IV; R = Ph). The dibenzylamino-cyanide gave also 1-benzyl-2-imino-3-phenylpyrrolidine (II; R = Ph, R′ = H, R″ = CH_2Ph) as the hydrochloride (34%), which was identified by conversion into the corresponding pyrrolidone. In acetic–hydrochloric acid, more benzyl chloride was formed (16 and 27%) respectively, and the yields of *tert.*-amino-acids fell. With one exception, mentioned above, 2-iminopyrrolidines or their transformation products were not isolated from these reactions, or from melts of the benzylmethylamino-cyanide toluene-*p*-sulphonate. The *γ-tert.*-amino-α-phenyl acid hydrochlorides were esterified very rapidly in alcohols containing free hydrogen chloride; in hot acetic anhydride (also when heated alone at 225°) they were cyclised to the two pyrrolidones (III; R = Ph, R′ = H, R″ = Me, and CH_2Ph). The second pyrrolidone was made also from α-phenyl-γ-butyrolactone and benzylamine.

Benzylmethylamine or dibenzylamine with 3-chloropropyl cyanide readily afforded the 3-dialkylaminopropyl cyanides (I; R = R′ = H, R″ = Me and CH_2Ph). These cyanides were hydrolysed rapidly in hot hydrochloric acid, yielding the *tert.*-amino-acids (IV; R = H). In acetic–hydrochloric acid, 1—3% of benzyl chloride was formed in each case; in aqueous media, there was no trace of benzyl chloride. The benzylmethylamino- and dibenzylamino-acid (IV; R = H) were synthesised independently from diethyl malonate and the 2-dialkylaminoethyl chlorides. These amino-acid hydrochlorides were readily converted by hot acetic anhydride into 1-methyl- and 1-benzyl-pyrrolid-2-ones (III; R = R′ = H, R″ = Me and CH_2Ph), benzyl chloride, and acetate. The infrared absorption of 1-benzylpyrrolid-2-one was identical with that of an authentic sample made from

γ-butyrolactone and benzylamine. These two pyrrolidones formed water-soluble salts with hydrochloric acid; so did *N*-benzyl-*N*-methylacetamide, which has a similar structure.

Ammonia was unexpectedly and rapidly evolved on treating benzylamine with 3-chloropropyl cyanide in alcohols, and 1-benzyl-2-benzyliminopyrrolidine (V) was obtained. This reaction could not be stopped at the evident intermediate stage (cf. the similar reaction described by King, Latham, and Partridge, *J.*, 1952, 4271). The pyrrolidine was stable to nitrous acid, and was not hydrolysed by acid. However, in hot alkali ring-scission occurred, and *N*-benzyl-γ-benzylaminobutyramide (VI) (56%) and a little benzylamine (22%) were formed. The structure of the amide follows from its synthesis from *N*-benzyl-γ-chlorobutyramide and benzylamine. Alkaline hydrolysis of the pyrrolidine evidently occurs by rupture of the >N–C< bond; the ring fission on hydrolysis of 2-alkyl-4 : 5-dihydroglyoxalines (cf., *e.g.*, Aspinall, *J. Org. Chem.*, 1941, **6**, 895) is probably similar.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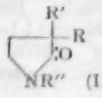
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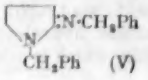
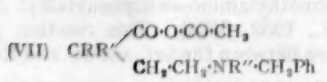

(V)

$CH_2Ph\cdot NH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO\cdot NH\cdot CH_2Ph$ (VI)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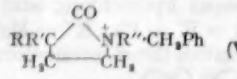
(VIII)

Discussion.—The experimental results indicate that the debenzylation by hydrochloric acid competes with ordinary hydrolysis of the cyano-group. The effect of acetic acid in promoting debenzylation may be due to the lowered dielectric constant of the media, which would assist an intramolecular interaction. It is well known that αα-diphenylalkyl cyanides resist hydrolysis, probably because of steric hindrance, and in this series, debenzylation and iminopyrrolidine formation are virtually complete. The other basic cyanides studied have a single α-phenyl substituent, or none; they are mainly hydrolysed by hydrochloric acid to the *tert.*-amino-acids, although under favourable conditions (*e.g.*, in acetic acid) a little benzyl chloride is also formed. The probable mechanism by which a cyano-group activates a suitably placed benzyl–nitrogen bond (Wilson, *locc. cit.*) suggests that carbonyl and carboxyl groups would not have the same effect. In accordance with this, 4-dibenzylaminopentan-2-one and γ-*tert.*-benzylamino-acids are stable in boiling hydrochloric acid; benzyltriethylammonium chloride is also stable under these conditions.

During the present work, several γ-*tert.*-benzylamino-acid hydrochlorides were cyclised to pyrrolidones by hot acetic anhydride. This debenzylation (benzyl chloride and acetate are formed) possibly proceeds *via* a mixed anhydride (VII), and the ion (VIII), which should decompose into a pyrrolidone and a benzyl cation (cf. *J.*, 1952, 3526).

Experimental

3-*Dibenzylamino*-1 : 1-*diphenylpropyl Cyanide*.—The hydrochloride (m. p. 188°; 53% yield) and the base (m. p. 60—61°) were made following Dupré, Elks, Hems, Speyer, and Evans (*J.*, 1949, 504). The intermediate 2-dibenzylaminoethyl chloride formed a *picrate*, m. p. 123° (Found: N, 11·2. $C_{16}H_{18}NCl,C_6H_3O_7N_3$ requires N, 11·45%).

Debenzylation of **3-*Dibenzylamino*-1 : 1-*diphenylpropyl Cyanide*.**—(*a*) The hydrochloride (3 g.) and concentrated hydrochloric acid (40 c.c.) were refluxed for 48 hr., more acid (50 c.c.) being added during this period. The hydrochloride slowly dissolved, and a volatile oil separated. Steam-distillation gave benzyl chloride (0·4 g., 48%; characterised as *S*-benzylthiuronium picrate). The residual solution was concentrated, and concentrated hydrochloric acid added to precipitate crystals (1·2 g.; m. p. 273°). Recrystallisation from 15% hydrochloric acid gave **1-*benzyl*-2-*imino*-3 : 3-*diphenylpyrrolidine hydrochloride*** (1·1 g., 47%) as needles, m. p. 292—293° (Found: C, 76·35; H, 6·25. $C_{23}H_{23}N_2HCl$ requires C, 76·15; H, 6·4%).

(*b*) A mixture of glacial acetic acid (30 c.c.), concentrated hydrochloric acid (50 c.c.), and

the dibenzylamino-compound hydrochloride (3 g.) was refluxed for 7 hr., evaporated to small bulk, and treated with 15% hydrochloric acid (100 c.c.), yielding the iminopyrrolidine hydrochloride (2·0 g., 84%), m. p. 292—293°. This with aqueous potassium nitrate gave the *iminopyrrolidine nitrate*, m. p. 221—222° (Found: N, 10·65. $C_{23}H_{22}N_2.HNO_3$ requires N, 10·8%), only slightly soluble in cold water. The nitrate was also obtained from the iminopyrrolidine hydrochloride, aqueous acetic acid, sodium nitrite, and hydrochloric acid at 60°. However, boiling the hydrochloride for 2 min. with sodium nitrite in aqueous acetic acid gave *1-benzyl-3 : 3-diphenylpyrrolid-2-one*, m. p. 93—94° (from aqueous methanol) (Found: N, 3·9. $C_{23}H_{21}ON$ requires N, 4·25%), which was insoluble in dilute hydrochloric acid. The iminopyrrolidine hydrochloride (420 mg.) was boiled with acetic anhydride (4 c.c.) for 5 min., then water was added. Crystallisation of the product from aqueous ethanol gave *2-acetimido-1-benzyl-3 : 3-diphenylpyrrolidine* (0·4 g., 92%) as plates, m. p. 121° (Found: C, 81·45; H, 6·9. $C_{25}H_{24}ON_2$ requires C, 81·5; H, 6·6%), which dissolved in 2N-hydrochloric acid.

3-Dibenzylamino-1-phenylpropyl Cyanide.—2-Dibenzylaminoethyl chloride (36·4 g.) was treated with benzyl cyanide (14·4 g.) in dry benzene (180 c.c.) in the presence of sodamide (4·9 g.) at 40°, the reaction being completed at 80° for 2 hr. After washing with water, distillation gave *3-dibenzylamino-1-phenylpropyl cyanide* (32 g., 67%), b. p. 164—168°/10^{-4} mm. (Found, on material regenerated from the oxalate: N, 8·2. $C_{24}H_{24}N_2$ requires N, 8·25%). The *hydrogen oxalate*, recrystallised from acetone–ether, had m. p. 134—135° (Found: C, 72·2; H, 6·0. $C_{24}H_{24}N_2.H_2C_2O_4$ requires C, 72·5; H, 6·1%). The cyanide (2·8 g.), concentrated hydrochloric acid (30 c.c.), and acetic acid (10 c.c.) were refluxed for 1 hr. The solution was evaporated to dryness and the product washed with a little chloroform. Recrystallisation from 15% hydrochloric acid gave *γ-dibenzylamino-α-phenylbutyric acid hydrochloride* (1·4 g., 60%), m. p. 202—204° (Found: N, 3·35. $C_{24}H_{25}O_2N,HCl$ requires N, 3·55%). The original distillate gave benzyl chloride (280 mg., 27%) on neutralisation with sodium hydrogen carbonate and ether-extraction.

1-Benzyl-2-imino-3-phenylpyrrolidine Hydrochloride.—3-Dibenzylamino-1-phenylpropyl cyanide (1 g.) was refluxed with concentrated hydrochloric acid (20 c.c.) for 6 hr. Benzyl chloride (54 mg., 15%) was isolated; the aqueous solution was evaporated to 10 c.c. and water (10 c.c.) added. The crystals of γ-dibenzylamino-α-phenylbutyric acid hydrochloride (0·64 g., 55%), m. p. 202—204°, were filtered off. Evaporation of the filtrate and recrystallisation from ethanol–ether gave *1-benzyl-2-imino-3-phenylpyrrolidine hydrochloride* (0·28 g., 34%), m. p. 206—208° (Found: N, 9·75. $C_{17}H_{18}N_2,HCl$ requires N, 9·75%). The m. p. was depressed to 185° on admixture with the amino-acid hydrochloride. The pyrrolidine hydrochloride was dissolved in acetic acid, aqueous sodium nitrite added, and the mixture boiled for 2 min., to give 1-benzyl-3-phenylpyrrolid-2-one, m. p. and mixed m. p. 99° (cf. below).

1-Benzyl-3-phenylpyrrolid-2-one.—(*a*) γ-Dibenzylamino-α-phenylbutyric acid hydrochloride was heated at 220—230° for 1 hr. The dark product, recrystallised from ethanol (charcoal), gave the *pyrrolidone* (5%), m. p. 101—102° (Found: C, 81·2; H, 6·9. $C_{17}H_{17}ON$ requires C, 81·25; H, 6·8%). (*b*) The same hydrochloride (420 mg.) was boiled with acetic anhydride (10 c.c.) for 5 min. The anhydride was removed at 20 mm. and the residue recrystallised from aqueous ethanol, yielding the pyrrolidone (200 mg., 100%), m. p. 101—102°. (*c*) 3-Hydroxy-1-phenylpropyl cyanide (35%), b. p. 137—141°/0·01 mm., was made by a method similar to that employed by King, Latham, and Partridge (*J.*, 1952, 4269), except that benzene was the sole solvent used. This cyanide (9·8 g.), concentrated hydrochloric acid (60 c.c.), and water (10 c.c.) were refluxed for 12 hr.; ether-extraction gave α-phenyl-γ-butyrolactone (6·1 g., 62%), b. p. 118—129°/0·01 mm. (Rothstein, *Bull. Soc. chim. France*, 1935, 80, gives b. p. 178°/13·5 mm.; McElvain and Laughton, *J. Amer. Chem. Soc.*, 1951, 73, 451, give b. p. 131—134°/0·3 mm.). The lactone (1·5 g.), benzylamine (10 c.c.) and concentrated hydrochloric acid (0·5 c.c.) were heated at 180° for 12 hr. The residue, after extraction with dilute acetic acid, recrystallised from aqueous ethanol, yielding the pyrrolidone (1·9 g., 78%), m. p. 101—102°.

3-Benzylmethylamino-1-phenylpropyl Cyanide.—This cyanide (b. p. 141—144°/0·01 mm.; 62% yield; Bergel, Hindley, Morrison, and Rinderknecht, U.S.P. 2,405,555; *Chem. Abs.*, 1947, 41, 159; Kägi and Miescher, *Helv. Chim. Acta*, 1949, 32, 2498) gave a *hydrochloride*, m. p. 140—142° (Found: N, 9·25. $C_{18}H_{20}N_2,HCl$ requires N, 9·3%). The *hydrogen oxalate*, m. p. 121—123°, was recrystallised from acetone–ether (Found: C, 67·7; H, 6·1. $C_{18}H_{20}N_2.H_2C_2O_4$ requires C, 67·8; H, 6·25%). The *toluene-p-sulphonate* had m. p. 144—146° (from ethanol–ether) (Found: N, 6·25. $C_{18}H_{20}N_2.C_7H_8O_3S$ requires N, 6·4%).

Attempted Debenzylation of 3-Benzylmethylamino-1-phenylpropyl Cyanide.—(*a*) The cyanide (5·3 g.) and concentrated hydrochloric acid (50 c.c.) were refluxed for 3 hr. Only traces of

benzyl chloride were formed. The solution was evaporated to dryness and the residue recrystallised from aqueous hydrochloric acid, giving *γ-benzylmethylamino-α-phenylbutyric acid hydrochloride* (6·2 g., 97%), m. p. 202—204° (Found: N, 4·4. $C_{18}H_{21}O_2N$,HCl requires N, 4·4%).

(*b*) The cyanide hydrochloride (3·35 g.), concentrated hydrochloric acid (25 c.c.), and acetic acid (25 c.c.) were refluxed for 7 hr. (liquid temp. 107°), to give γ-benzylmethylamino-α-phenylbutyric acid hydrochloride (2·3 g., 65%), m. p. 202°, and benzyl chloride (250 mg., 18%). In a similar hydrolysis, the crude product from 3·3 g. of cyanide was dissolved in methanol (25 c.c.), and a little ether was added; ammonium chloride (0·5 g., 72%) was filtered off. The methanol was evaporated and the residue dissolved in cold water and basified, liberating as an oil *methyl γ-benzylmethylamino-α-phenylbutyrate* (1·6 g., 43%), b. p. 118—120°/0·01 mm. (Found: N, 4·65. $C_{19}H_{23}O_2N$ requires N, 4·7%). The ester (800 mg.) and 15% hydrochloric acid (25 c.c.), refluxed for 8 hr., gave γ-benzylmethylamino-α-phenylbutyric acid hydrochloride (600 mg., 70%), m. p. 201°.

(*c*) The cyanide toluene-*p*-sulphonate was heated at 200° for 4 hr.; trituration with acetone gave unchanged toluene-*p*-sulphonate (90%). A similar fusion in the presence of free toluene-*p*-sulphonic acid gave a resin.

1-Methyl-3-phenylpyrrolid-2-one.—γ-Benzylmethylamino-α-phenylbutyric acid hydrochloride (2 g.) and acetic anhydride (20 c.c.) were refluxed for 30 min., the anhydride distilled off, and the residue recrystallised from light petroleum (b. p. 40—60°)–benzene. The *pyrrolidone* (220 mg., 20%) had m. p. 58—59° (Found: N, 7·8. $C_{11}H_{13}ON$ requires N, 8·0%). Benzyl chloride was identified in the distillate.

3-Dibenzylaminopropyl Cyanide.—3-Chloropropyl cyanide (yield 61%; b. p. 71—74°/8 mm.; Whitmore *et al.*, *J. Amer. Chem. Soc.*, **1944**, **66**, 730) (5·1 g.), dibenzylamine (20 g.), sodium iodide (50 mg.), and anisole (25 c.c.) were refluxed for 3 hr., then light petroleum (b. p. 60—80°) (50 c.c.) was added. Dibenzylammonium chloride (10·4 g.) was filtered off, and the solution distilled, yielding *3-dibenzylaminopropyl cyanide* (8·1 g., 63%), b. p. 152—155°/0·01 mm., m. p. 45—46° (from light petroleum, b. p. 40—60°) (Found: N, 10·3. $C_{18}H_{20}N_2$ requires N, 10·6%). The hydrochloride and picrate were syrups; the *hydrogen oxalate* formed rosettes, m. p. 142—144° from acetone (Found: N, 7·7. $C_{18}H_{20}N_2,H_2C_2O_4$ requires N, 7·9%).

Hydrolysis of 3-Dibenzylaminopropyl Cyanide.—(*a*) The cyanide (1 g.) and concentrated hydrochloric acid (30 c.c.) were boiled for 3 hr. No benzyl chloride was detected; the mixture was evaporated to dryness under reduced pressure, concentrated aqueous ammonia (10 c.c.) added, and the mixture again evaporated. The solid was extracted with hot chloroform, the ammonium chloride being filtered off. Evaporation of the chloroform gave the crude amino-acid as a syrup; treatment with ethereal hydrogen chloride and recrystallisation from acetone–ethanol gave *γ-dibenzylaminobutyric acid hydrochloride* (1 g., 83%), m. p. 122—126° (Found: N, 4·4. $C_{18}H_{21}O_2N$,HCl requires N, 4·4%).

(*b*) The cyanide (3·7 g.), acetic acid (10 c.c.), and hydrochloric acid (30 c.c.) were refluxed for 2 hr., affording benzyl chloride (53 mg., 3%) and γ-dibenzylaminobutyric acid hydrochloride (3·4 g., 76%), m. p. 122—124° after recrystallisation from ethanol–ether.

Independent Synthesis of γ-Dibenzylaminobutyric Acid Hydrochloride.—Diethyl sodiomalonate was treated with 2-dibenzylaminoethyl chloride, as described below for the benzylmethylamino-analogue. The crude diethyl 2-dibenzylaminoethylmalonate decomposed on attempted distillation at 10^{-4} mm. (The ester has been made by Eisleb and Ehrhart, G.P., 550,762; *Chem. Zentr.*, 1932, II, 615.) The crude ester (3·3 g.), glacial acetic acid (10 c.c.), and concentrated hydrochloric acid (20 c.c.) were refluxed for 12½ hr., and gave γ-dibenzylaminobutyric acid hydrochloride (1·6 g., 57%), m. p. 124—126°.

3-Benzylmethylaminopropyl Cyanide.—A mixture of benzylmethylamine (15·8 g.), 3-chloropropyl cyanide (6·75 g.), sodium iodide (50 mg.), and toluene (50 c.c.) was refluxed for 4 hr., washed with water and distilled, yielding *3-benzylmethylaminopropyl cyanide* (8 g., 65%), b. p. 150—151°/1 mm. (Found: N, 14·5. $C_{12}H_{16}N_2$ requires N, 14·9%). The hydrochloride was a syrup, and the *hydrogen oxalate* formed rosettes m. p. 136—137°, from acetone–ethanol (Found: N, 10·4. $C_{12}H_{16}N_2,H_2C_2O_4$ requires N, 10·1%).

Hydrolysis of 3-Benzylmethylaminopropyl Cyanide.—(*a*) The cyanide (2 g.) and concentrated hydrochloric acid (30 c.c.) were refluxed for 3 hr. No benzyl chloride was formed. The solution was evaporated almost to dryness at 15 mm., concentrated ammonia solution (10 c.c.) added, and the whole again evaporated. The free amino-acid was extracted into chloroform and treated with ethereal hydrogen chloride, to yield *γ-benzylmethylaminobutyric acid hydrochloride* (2·3 g., 89%), m. p. 168—169° (Found: N, 5·55. $C_{12}H_{17}O_2N$,HCl requires N, 5·75%). The m. p. was not depressed on admixture with a specimen prepared from malonic ester (see below).

(*b*) The cyanide (3 g.), acetic acid (10 c.c.), and concentrated hydrochloric acid (30 c.c.) were refluxed for 2 hr., and yielded benzyl chloride (30 mg., 1½%).

Independent Synthesis of γ-Benzylmethylaminobutyric Acid Hydrochloride.—Diethyl malonate (23·5 g.), then a solution of 2-benzylmethylaminoethyl chloride (22·5 g.) in ethanol (50 c.c.), were added in quick succession to a solution of sodium (3·0 g.) in anhydrous ethanol (100 c.c.) at 20°. The mixture was refluxed for 3 hr., evaporated, diluted with water, and extracted with ether–benzene, to give *diethyl 2-benzylmethylaminoethylmalonate* (17 g., 46%), b. p. 135—136°/0·01 mm. (Found: N, 4·65. $C_{17}H_{25}O_4N$ requires N, 4·55%). The ester (6·2 g.), acetic acid (15 c.c.), and concentrated hydrochloric acid (30 c.c.) were refluxed for 18 hr.; evaporation and recrystallisation from ethanol–ether gave γ-benzylmethylaminobutyric acid hydrochloride (4·7 g.), m. p. 170—172°.

1-*Methylpyrrolid-2-one.*—The foregoing hydrochloride (4·7 g.) and acetic anhydride (30 c.c.) were boiled for 3½ hr. The anhydride was distilled off, and dilute hydrochloric acid added; benzyl chloride and acetate were removed by ether-extraction. The aqueous solution was basified and extracted with ether, yielding 1-methylpyrrolid-2-one (1 g., 52%), b. p. 71—72°/12 mm. (Prill and McElvain, *J. Amer. Chem. Soc.*, 1933, **55**, 1241, give b. p. 84—85°/14 mm.; Craig, *ibid.*, p. 297, b. p. 94—96°/20 mm.). Ethereal hydrogen chloride gave the hydrochloride, which formed needles, m. p. 85—87°, from acetone–ether (McElvain and Vozza, *ibid.*, 1949, **71**, 897, give m. p. 86—88°). Similarly *N*-benzyl-*N*-methylacetamide formed a *hydrochloride*, m. p. 129° (Found: N, 7·25. $C_{10}H_{13}ON$,HCl requires N, 7·0%).

1-*Benzylpyrrolid-2-one.*—(*a*) The following is a modification of the method described by Späth and Lintner (*Ber.*, 1936, **69**, 2730). γ-Butyrolactone (12·9 g.), benzylamine (80 c.c.), and benzylammonium chloride (2·5 g.) were refluxed for 16 hr., cooled, and made strongly alkaline with 10N-sodium hydroxide. Ether-extraction and distillation afforded benzylamine and a residue of *N*-benzyl-γ-hydroxybutyramide (14·6 g., 47%), m. p. 74° (Späth and Lintner, *loc. cit.*, give m. p. 74—75°). The benzylamide (10 g.) and benzylammonium chloride (0·5 g.) were heated at 280° (dimethyl phthalate vapour bath) for 1 hr. The product was dissolved in ether, washed with aqueous sodium hydroxide, and distilled, yielding 1-benzylpyrrolid-2-one (8·3 g., 92%), b. p. 112—115°/0·08 mm., n_D^{20} 1·5550 (Späth and Lintner, *loc. cit.*, give b. p. 130—140°/1 mm.; Iselin and Hofmann, *Helv. Chim. Acta*, 1954, **37**, 178, b. p. 112—113°/0·08 mm.). The pyrrolidone gave a syrupy, water-soluble hydrochloride.

(*b*) γ-Dibenzylaminobutyric acid hydrochloride (3·7 g.) and acetic anhydride (30 c.c.) were heated at 100° for 1 hr., then refluxed for ½ hr. Acetic anhydride was distilled off at 15 mm. and the residue stirred with 2N-hydrochloric acid (20 c.c.) and extracted with ether. The pyrrolidone was liberated by adding potassium carbonate to the aqueous layer; it had b. p. 112—113°/0·08 mm., n_D^{20} 1·5478 (yield, 1·4 g., 78%). The infrared absorption over the range 1800—750 cm.$^{-1}$ of the pyrrolidone samples prepared by methods (*a*) and (*b*) were almost identical; there was a broad, strong CO stretching band at 1690 cm.$^{-1}$ (cf. the 1700-cm.$^{-1}$ band in pyrrolidone, quoted by Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1954, p. 183).

1-*Benzyl-2-benzyliminopyrrolidine.*—3-Chloropropyl cyanide (4·7 g.) propan-1-ol (20 c.c.), sodium iodide (50 mg.), and benzylamine (9·4 g.) were refluxed for 8 hr.; ammonia was copiously evolved. The basic product was separated and treated with ethereal hydrogen chloride, yielding 1-*benzyl-2-benzyliminopyrrolidine hydrochloride* (9·4 g., 68%), m. p. 187—188° (Found: N, 9·0. $C_{18}H_{20}N_2$,HCl requires N, 9·3%). The *picrate* had m. p. 136° (Found: N, 14·15. $C_{18}H_{20}N_2$,$C_6H_3O_7N_3$ requires N, 14·2%); the *nitrate*, m. p. 147—148° (Found: N, 12·55. $C_{18}H_{20}N_2$,HNO_3 requires N, 12·85%), was almost insoluble in cold water. The hydrochloride was unchanged after 17 hours' refluxing with concentrated hydrochloric acid. A mixture of the hydrochloride (2 g.), ethanol (10 c.c.), and 5N-sodium hydroxide (10 c.c.) was refluxed for 10½ hr. The ethanol was distilled off and treated with hydrogen chloride, affording benzylammonium chloride (200 mg., 22%). The mixture was extracted with ether, and ethereal hydrogen chloride added. Recrystallisation of the product from ethanol or water afforded *N-benzyl-γ-benzylaminobutyramide hydrochloride* (1·2 g., 56%), m. p. 211—213° (Found: N, 9·0. $C_{18}H_{22}ON_2$,HCl requires N, 8·8%).

Independent Synthesis of N-Benzyl-γ-benzylaminobutyramide.—γ-Butyrolactone (20 g.) and concentrated hydrochloric acid (100 c.c.) were refluxed for 16 hr., yielding γ-chlorobutyric acid (4·3 g., 15%), b. p. 67—70°/0·1 mm. (cf. Cloves, *Annalen*, 1901, **319**, 360). The chloro-acid was converted *via* the acid chloride into γ-chlorobutyrobenzylamide (63%), m. p. 67° (Hanford and Adams, *J. Amer. Chem. Soc.*, 1935, **57**, 924, give m. p. 68°). The chloro-amide (1·1 g.) benzylamine (0·58 g.), sodium iodide (10 mg.), and ethanol (20 c.c.) were refluxed for 8 hr., and

ether was added. *N*-Benzyl-γ-benzylaminobutyramide hydrochloride (0·4 g., 24%), separated as needles, m. p. 211—213°.

4-Dibenzylaminopentan-2-one.—Ethyl acetoacetate (10 g.) was added to a solution of sodium (1·95 g.) in ethanol (100 c.c.). 2-Dibenzylaminoethyl chloride (22 g.) was then added dropwise during 1 hr. to the boiling mixture. After 4 hours' further refluxing, the mixture was filtered and evaporated. The crude oxo-ester (15 g.) was stirred with a solution of potassium hydroxide (2·5 g.) in ethanol (30 c.c.) and water (100 c.c.) at 20° for 4 hr. A slight excess of 2N-hydrochloric acid was added and the solution heated at 70° to expel carbon dioxide. Excess of 10N-sodium hydroxide was added, and the basic ketone (7·4 g., 60%), b. p. 138—145°/0·01 mm., was isolated by ether-extraction (Eisleb and Ehrhart, *loc. cit.*, give b. p. 185—195°/3 mm., for this compound, made by a related procedure). 4-Dibenzylaminopentan-2-one was refluxed with concentrated hydrochloric acid for 6 hr.; no benzyl chloride was formed. Benzyltriethylammonium chloride was recovered unchanged after being boiled for 3 hr. with concentrated hydrochloric acid; no benzyl chloride was formed.

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*Additive Compounds as Possible Intermediates in Substitution Processes. Part II.**

By F. BELL.

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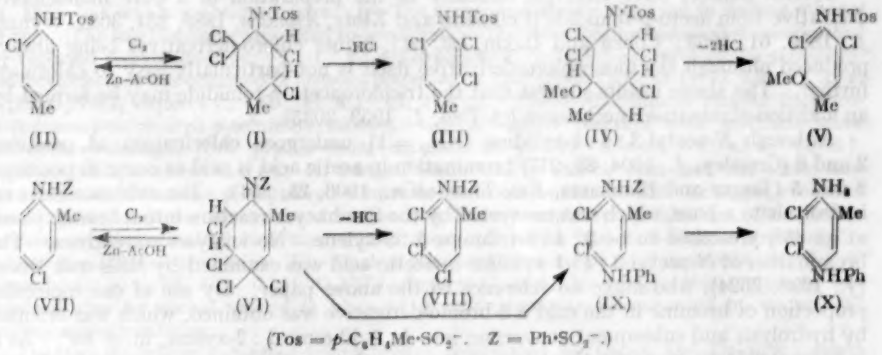
Derivatives of *cyclo*hexene are readily produced by the chlorination of many sulphonanilides. The reactions of these compounds are described. Observations are recorded on the halogenation of 3 : 4 : 1-xylidine.

SCHULOFF, POLLAK, AND RIESS (*Ber.*, 1929, **62**, 1849), by the treatment of toluene-*p*-sulphonyl-*p*-toluidine with excess of chlorine, obtained a compound, m. p. 176°, which was not analysed but was found to yield with 80% sulphuric acid a trichloro-*p*-toluidine, m. p. 59—60°. Bell (*J.*, 1953, 4182) recorded that the analysis of the above compound, after purification, corresponded to that of a tetrachloro-derivative but it is now confirmed that hydrolysis yields a trichloro-base. More detailed examination leads to the unusual constitution (I) for this compound and not *N* : 2 : 3 : 6-tetrachloro-*N*-(toluene-*p*-sulphonyl)-*p*-toluidine ($NH_2 = 1$) (see Chattaway, *J.*, 1904, **85**, 1185, for properties of *N*-chlorosulphonamides). The compound reacts vigorously with piperidine or aniline, indicating the presence of reactive chlorine. On reduction with zinc and acetic acid it gives 2-chloro-*N*-(toluene-*p*-sulphonyl)-*p*-toluidine (II), whereas related nuclear halogenated compounds, such as 2-bromo-6-chloro- and 2 : 6-dibromo-*N*-(toluene-*p*-sulphonyl)-*p*-toluidines, are unchanged under the same conditions. The tetrachloro-compound is smoothly decomposed by heat to yield 2 : 3 : 6-trichloro-*N*-(toluene-*p*-sulphonyl)-*p*-toluidine (III), also obtained, but in small yield, by dissolving the tetrachloro-compound in pyridine. When boiled with alcohols the tetrachloro-compound gave the trichloro-compound (III) together with addition products, probably of type (IV) (position of OMe uncertain), which were converted almost quantitatively into compounds of type (V) by dissolution in pyridine.

The trichloro-compound (III) was smoothly hydrolysed to 2 : 3 : 6-trichloro-*p*-toluidine, m. p. 60—62°, which formed an acetyl derivative, m. p. 196°. As Cohen and Dakin (*J.*, 1902, **81**, 1337) give m. p. 179° for the trichloro-derivative formed by the prolonged action of sodium chlorate and hydrochloric acid on aceto-*p*-toluidide and this value appears to be confirmed by Mannino and Di-Donato (*Gazzetta*, 1908, **38**, 22), who used a mixture of concentrated hydrochloric acid and nitric acid to chlorinate aceto-*p*-toluidide, both processes were re-examined. Cohen and Dakin's method gave material of rather indefinite

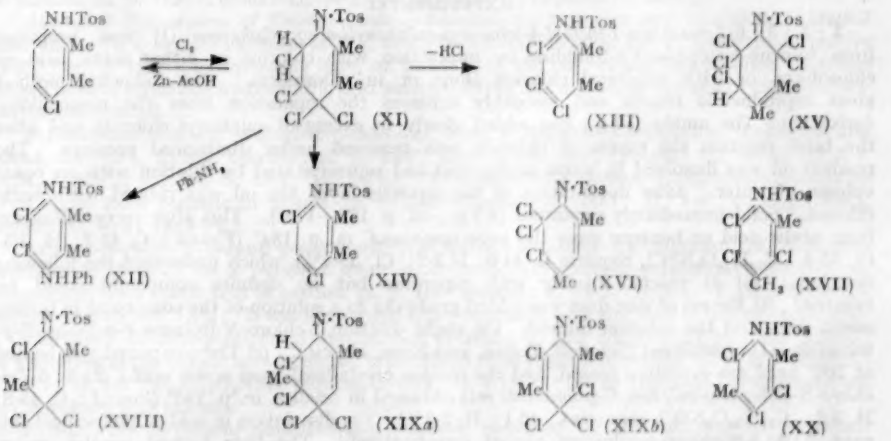
* Part I, *J.*, 1955, 24.

m. p., which on hydrolysis gave a base requiring purification by recrystallisation. The pure base gave an acetyl derivative, m. p. 196°, identical with the above. Mannino and Di-Donato's method yielded in our hands none of the desired trichloro-derivative although it is clear that the authors themselves handled the pure trichloro-base.



Chlorination of benzenesulphonyl-*p*-toluidine gave a compound analogous to (I), and of benzenesulphonyl-*o*-toluidine a compound to which is ascribed formula (VI). The latter product was decomposed by heat to the trichloro-compound (VIII), and was smoothly reduced to *N*-benzenesulphonyl-4-chloro-*o*-toluidine ($NH_2 = 1$) (VII); with aniline it gave the derivative (IX), which was readily hydrolysed to the dichlorodiamine (X).

Similar results were obtained with certain xylidines. 2 : 3 : 1-Xylidine gave the compound to which is ascribed formula (XI), and the reactions of which are set out. The



smooth reaction with aniline to yield the compound (XII), the conversion into the trichloro-derivative by boiling alcohol, and the production of both the trichloro- (XIII) and the dichloro-derivative (XIV) by dissolution in pyridine are worthy of note. 3 : 4 : 1-Xylidine gave in very small yield a compound, probably (XV), which was not examined in detail. 1 : 3 : 2-Xylidine gave substitution products together with uncrystallisable oils. 2 : 4 : 1-Xylidine gave in small yield a reactive trichloro-compound, probably (XVI), together with the aromatic isomer (XVII). *p*-Xylidine gave a mixture of a trichloro- and a tetrachloro-compound. The trichloro-compound, probably (XVIII), passed rapidly in

hot ethanol into the aromatic product (XX). The tetrachloro-compound, probably (XIX *a* or *b*), was stable under the same conditions. It appears from these results that a methyl group in the benzene nucleus usually opposes the addition of chlorine to the carbon atom to which it is itself attached.

Several authors have recorded difficulty in the preparation of a pure monochloro-derivative from aceto-*p*-toluidide (Lellmann and Klotz, *Annalen*, 1885, **231**, 308; Wynne, *J.*, 1892, **61**, 1053; Cohen and Dakin, *loc. cit.*), higher chloro-derivatives being always produced although the monochloro-derivative itself is not particularly easy to chlorinate further. The above results suggest that the trichloroaceto-*p*-toluidide may be formed by an addition-elimination mechanism (cf. Bell, *J.*, 1953, 3035).

Although *N*-acetyl-3 : 4 : 1-xylidine ($NH_2 = 1$) undergoes chlorination at positions 2 and 6 (Crossley, *J.*, 1904, **85**, 277) bromination in acetic acid is said to occur in positions 2 and 5 (Jaeger and Blanksma, *Rec. Trav. chim.*, 1906, **25**, 354). The evidence rests on hydrolysis to a base, which was converted by the Sandmeyer reaction into a bromoxylene, m. p. 86°, presumed to be 3 : 4 : 6-tribromo-1 : 2-xylene. No analyses were given. The bromination of *N*-acetyl-3 : 4 : 1-xylidine in acetic acid was examined by Mills and Nixon (*J.*, 1930, 2524), who make no reference to the above paper. By use of one molecular proportion of bromine in the cold a 6-bromo-derivative was obtained, which was oriented by hydrolysis and subsequent conversion into 4 : 5-dibromo-1 : 2-xylene, m. p. 88°. As it is not possible to reconcile these two statements the reaction was re-examined. It was found that the 6-bromo-derivative was the only product even when a very large excess of bromine was employed. *N*-Toluene-*p*-sulphonyl-3 : 4 : 1-xylidine behaved similarly, and only in pyridine did it undergo dibromination, then giving the 2 : 6-dibromo-derivative. It is concluded the Jaeger and Blanksma's "3 : 4 : 6-tribromo-1 : 2-xylene" was in fact 4 : 5-dibromo-1 : 2-xylene, and that bromination of derivatives of 3 : 4 : 1-xylidine follows the same course as chlorination, but that the 2-position is entered with considerably greater difficulty.

Experimental

3 : 3 : 5 : 6-*Tetrachloro*-1-*methyl*-4-*toluene*-p-*sulphonyliminocyclohexene* (I) was prepared from toluene-*p*-sulphonyl-*p*-toluidine by interaction with chlorine in either acetic acid or chloroform, or with sulphuryl chloride alone or in chloroform. The following method gives reproducible results and smoothly achieves the separation from the monochloro-derivative. The amide (10 g.) was added slowly to excess of sulphuryl chloride and after the brisk reaction the excess of chloride was removed under diminished pressure. The residual oil was dissolved in warm acetic acid and reprecipitated by dilution with an equal volume of water. After decantation of the aqueous layer the oil was rubbed with warm ethanol. Solid immediately separated (4·7 g.; m. p. 175—179°). This after recrystallisation from acetic acid or benzene gave the pure *compound*, m. p. 184° (Found: C, 42·3; H, 3·3; Cl, 35·4. $C_{14}H_{12}O_2NSCl_4$ requires C, 41·9; H, 3·2; Cl, 35·4%), which underwent the following reactions: (*a*) It reacted readily with piperdine but no definite compound could be isolated. (*b*) Excess of zinc dust was added gradually to a solution of the compound in boiling acetic acid, and the solution filtered. On slight dilution 2-chloro-*N*-(toluene-*p*-sulphonyl)-*p*-toluidide (II) crystallised (Schuloff, Pollak, and Riess, *loc. cit.*). (*c*) The compound was heated at 200° until gas evolution ceased, and the residue crystallised from acetic acid. 2 : 3 : 6-*Trichloro*-*N*-(*toluene*-p-*sulphonyl*)-p-*toluidide* was obtained in needles, m. p. 160° (Found: C, 45·8; H, 3·2. $C_{14}H_{12}O_2NSCl_3$ requires C, 46·1; H, 3·3%). On dissolution in cold sulphuric acid this gave 2 : 3 : 6-trichloro-*p*-toluidine almost quantitatively. The base formed needles, m. p. 60—62°, from methanol, and on acetylation with cold acetic anhydride–concentrated sulphuric acid gave the acetyl or in the hot the *diacetyl derivative*, crystallising from acetic acid in needles, m. p. 196° (Found: C, 43·0; H, 3·4. Calc. for $C_9H_8ONCl_3$: C, 42·8; H, 3·2%) and 150° (Found: C, 45·2; H, 3·3. $C_{11}H_{10}O_2NCl_3$ requires C, 44·8; H, 3·4%) respectively. (*d*) The compound reacted vigorously with pyridine. On acidification of the solution 2 : 3 : 6-trichloro-*N*-(toluene-*p*-sulphonyl)-*p*-toluidine (above) was precipitated but in poor yield. (*e*) The compound (2 g.) was heated at 150° for 1½ hr. with sulphuric acid (4 c.c.) and water (4 c.c.), and the aqueous layer decanted from the black tar. Excess of aqueous ammomia was added and the product crystallised from aqueous methanol, to give trichlorotoluidine as above

(confirmed by preparation of acetyl and diacetyl derivatives). (*f*) On addition to aniline there was a very brisk reaction and the mixture set to a paste. Excess of aniline was removed by dilute hydrochloric acid, and the resultant pale yellow precipitate filtered off and dried. The product was extremely soluble in benzene or ethanol; it gave a clear solution in cold acetic acid which soon deposited a white solid. This recrystallised from acetic acid as needles, m. p. *ca.* 135°, but was not obtained pure. (*g*) The compound slowly dissolved in boiling ethanol (3 hr.). The solution was evaporated to small bulk. The crop obtained on cooling was purified by repeated recrystallisation. **1 : 1 : 3 : 4-*Tetrachloro*-6(?)*ethoxy*-5-*methyl*-2-*toluene*-p-*sulphonimido*cyclo*hexane*** was obtained in lustrous plates, m. p. 195° (Found: C, 43·1; H, 3·9; Cl, 32·4. $C_{16}H_{19}O_3NSCl_4$ requires C, 43·0; H, 4·2; Cl, 31·8%). The mother-liquors yielded trichloro-*N*-(toluene-*p*-sulphonyl)-*p*-toluidine (above). (*h*) A similar reaction with methanol gave the ***methoxy-analogue*** (IV), prisms (from ethanol), m. p. 187° (Found: C, 41·6; H, 3·7. $C_{15}H_{17}O_3NSCl_4$ requires C, 41·6; H, 3·9%). Reduction of this by zinc dust and acetic acid gave 2-chloro-*N*-(toluene-*p*-sulphonyl)-*p*-toluidine; decomposition at 220° until gas evolution ceased gave much tar and some trichloro-*N*-(toluene-*p*-sulphonyl)-*p*-toluidine. Dissolution in warm pyridine resulted in almost quantitative conversion into **2 : 6-*dichloro*-3-*methoxy*-N-(*toluene-p-sulphonyl*)-p-*toluidine*** (V), which crystallised from acetic acid in prisms, m. p. 190° (Found: C, 50·1; H, 4·2. $C_{15}H_{15}O_3NSCl_2$ requires C, 50·0; H, 4·2%); this compound was obtained also by use of aniline in place of pyridine but was accompanied by sticky, red decomposition products.

Trichloro-p-*toluidine*.—Aceto-*p*-toluidide was chlorinated by Cohen and Dakin's method (*loc. cit.*). The product had m. p. *ca.* 179° after crystallisation from acetic acid or chloroform (Cohen and Dakin give 179°) but was not pure. On hydrolysis in ethanol by hydrochloric acid it gave a base with a melting range 35—47°. This was purified by recrystallisation from light petroleum and then methanol, and then on re-acetylation gave trichloroaceto-*p*-toluidide, m. p. 196° (diacetyl derivative, m. p. 150°), identical with that described above. The base with toluene-*p*-sulphonyl chloride gave material which, after being freed from any ditoluene-*p*-sulphonyl derivative by dissolution in piperdine, crystallised from acetic acid to yield **2 : 3 : 6-**trichloro-*N*-(toluene-*p*-sulphonyl)-*p*-toluidine as prisms, m. p. 160° (above). Similarly there was obtained **2 : 3 : 6-*trichloro*-N-*benzenesulphonyl*-p-*toluidine***, which crystallised from ethanol in needles, m. p. 169° (Found: Cl, 30·2. $C_{13}H_{10}O_2NSCl_3$ requires Cl, 30·4%).

Attempted Preparation of Trichloro-aceto*-p-*toluidide by Mannino and Di-Donato's Method (loc. cit.).—In a typical experiment 5 g. of aceto-*p*-toluidide gave the 2 : 6-dinitro-derivative (1·9 g.), m. p. 190° (corresponding base, m. p. 168°), as the only crystalline product. Various proportions of nitric and hydrochloric acid were employed but in no case was any of the trichloro-derivative isolated.

N-*Benzenesulphonyl*-2 : 6-*dichloro*-p-*toluidine*, from 2 : 6-dichloro-*p*-toluidine (Lellmann and Klotz, *loc. cit.*), formed needles, m. p. 169°, from acetic acid (Found: C, 48·9; H, 3·8. $C_{13}H_{11}O_2NSCl_2$ requires C, 49·4; H, 3·5%). **2 : 6-*Dichloro*-N-(*toluene*-p-*sulphonyl*)-p-*toluidine*** crystallised from benzene in prisms, m. p. 180° (Found: C, 50·7; H, 3·9. $C_{14}H_{13}O_2NSCl_2$ requires C, 50·9; H, 3·9%).

2-*Bromo*-6-*chloro*-N-(*toluene*-p-*sulphonyl*)-p-*toluidine*, obtained by addition of *N*-bromosuccinimide (1 mol.) to a pyridine solution of 2-chloro-*N*-(toluene-*p*-sulphonyl)-*p*-toluidine, crystallised from acetic acid in needles, m. p. 180° (Found: C, 44·2; H, 3·3. $C_{14}H_{13}O_2NSClBr$ requires C, 44·8; H, 3·5%). It was unchanged after treatment with zinc dust in boiling acetic acid.

2-*Bromo*-N-(*toluene*-p-*sulphonyl*)-p-*toluidine*, obtained by the addition of bromine (1 mol.) to a solution of the anilide in chloroform, crystallised from ethanol in prisms, m. p. 118° (Found: C, 49·7; H, 4·3. $C_{14}H_{14}O_2NSBr$ requires C, 49·4; H, 4·1%). It was unchanged after treatment in chloroform with chlorine.

2 : 6-*Dibromo*-N-(*toluene*-p-*sulphonyl*)-p-*toluidine*, obtained by the addition of *N*-bromosuccinimide (2 mols.) to a pyridine solution of toluene-*p*-sulphonyl-*p*-toluidine, crystallised from acetic acid in needles, m. p. 179—180° (Found: Br, 38·7. $C_{14}H_{13}O_2NSBr_2$ requires Br, 38·2%), and was unchanged by zinc dust in acetic acid.

p-Toluidine treated with chlorine in acetic acid or under the conditions of D.R.-P. 400,254 gave thick, dark oils.

4-*Benzenesulphonylimino*-3 : 3 : 5 : 6-*tetrachloro*-1-*methyl*cyclo*hexene* (as I).—Excess chlorine was passed into a solution of benzenesulphonyl-*p*-toluidine in chloroform, and the solution diluted with light petroleum. The precipitated oil did not solidify for several days and was, therefore, separated and dissolved in ethanol. Crystals were soon formed and after recrystallisation from acetic acid gave the ***tetrachloro-compound*** as prisms, m. p. 164° (Found: Cl, 37·4.

$C_{13}H_{11}O_2NSCl_4$ requires Cl, 36·7%) (yield *ca.* 1 g. from 5 g.). This reacted vigorously with pyridine to give *N*-benzenesulphonyl-2 : 3 : 6-trichloro-*p*-toluidine (above) in small yield and with aniline to give a mixture from which was isolated a grey, crystalline powder, m. p. 158° (decomp.), by recrystallisation from acetic acid (Found: Cl, 30·4%); the latter appears to have been produced by removal of hydrogen chloride ($C_{19}H_{16}O_2NSCl_3$ requires Cl, 30·4%), but the product was of doubtful purity.

6-Benzenesulphonylimino-3 : 3 : 4 : 5-tetrachloro-1-methylcyclohexene (VI).—Excess of chlorine was passed into a solution of benzenesulphonyl-*o*-toluidine (4 g.) in chloroform, and the solution, after concentration, diluted with light petroleum. The crop (1·6 g.), after recrystallisation from acetic acid, gave the tetrachloro-compound as prisms, m. p. 166° (Found: Cl, 37·4. $C_{13}H_{11}O_2NSCl_4$ requires Cl, 36·7%). The yield was not improved by using *N*-benzenesulphonyl-4-chloro-*o*-toluidine as starting material. By zinc in acetic acid the tetrachloro-compound was smoothly converted into benzenesulphonyl-4-chloro-*o*-toluidine (VII). With aniline it reacted briskly to give *4-anilino-N-benzenesulphonyl-5 : 6-dichloro-o-toluidine* (IX), which formed prisms, m. p. 207°, from acetic acid (Found: C, 56·1; H, 3·8; Cl, 18·0. $C_{19}H_{16}O_2N_2SCl_2$ requires C, 56·0; H, 3·9; Cl, 17·4%), and was hydrolysed by cold sulphuric acid to *4-anilino-5 : 6-dichloro-o-toluidine* (X), which crystallised from ethanol in prisms, m. p. 115° (Found: C, 57·6; H, 4·1; Cl, 27·0. $C_{13}H_{12}N_2Cl_2$ requires C, 58·4; H, 4·5; Cl, 26·6%). When heated above the m. p., the tetrachloro-compound gave *N-benzenesulphonyl-4 : 5 : 6-trichloro-o-toluidine* (VIII), which crystallised from acetic acid in prisms, m. p. 159° (Found: Cl, 29·6. $C_{13}H_{10}O_2NSCl_3$ requires Cl, 30·4%).

Toluene-*p*-sulphonyl-*o*-toluidine (14 g.), submitted to the same process, gave the 4-chloro-derivative (4 g.) and an oil.

N-Acetyl-2-chloro-*p*-toluidine (4 g.) similarly gave the 2 : 6-dichloro-amide (1 g.) and an uncrystallisable oil.

Interaction of Arenesulphonamides with Sulphuryl Chloride.—Excess of sulphuryl chloride was added to the sulphonamide and, after the initial reaction, the excess of sulphuryl chloride was removed under diminished pressure and the residue (usually a glass) dissolved in ethanol or acetic acid.

The following results were obtained:

(*a*) Toluene-*p*-sulphonyl-*o*-toluidine (5 g.) gave the 4-chloro-derivative (4 g.), m. p. 144° (Schuloff, Pollak, and Riess, *loc. cit.*).

(*b*) Benzenesulphonyl-*o*-toluidine (4 g.) gave the 4-chloro-derivative (2·6 g.) and a small yield of the compound (VI), m. p. 166° (above).

(*c*) Benzenesulphonyl-*m*-toluidine gave an almost quantitative yield of the dichloro-derivative, m. p. 116° (Raper, Thompson, and Cohen, *J.*, 1904, **85**, 374).

(*d*) Toluene-*p*-sulphonyl-*m*-toluidine gave crude *2 : 4-dichloro-N-toluene-p-sulphonyl-m-toluidine*. The pure compound, prepared from 2 : 4-dichloro-*p*-toluidine, crystallised from acetic acid in prisms, m. p. 145° (Found: C, 50·3; H, 3·6. $C_{14}H_{13}O_2NSCl_2$ requires C, 50·9; H, 3·9%).

(*e*) Benzenesulphonyl-*p*-toluidine (5 g.) gave the 2-chloro-derivative (2·5 g.) and an oil.

(*f*) Toluene-*p*-sulphonyl-*p*-anisidine gave *dichloro-N-toluene-p-sulphonyl-p-anisidine*, which formed large prisms, m. p. 166°, from acetic acid (Found: Cl, 21·3. $C_{14}H_{13}O_3NSCl_2$ requires Cl, 20·5%). It was smoothly hydrolysed by cold sulphuric acid to the dichloro-base, needles (from aqueous methanol), m. p. 75° (Hodgson and Wignall, *J.*, 1927, 2219, give the m. p. of 2 : 6-dichloro-4-methoxyaniline as 71°; the 2 : 5-isomeride is not known.

Toluene-p-sulphonyl-2 : 3 : 1-xylidine, obtained by the interaction of 2 : 3 : 1-xylidine with toluene-*p*-sulphonyl chloride in pyridine, crystallised from ethanol in needles, m. p. 147° (Found: C, 65·6; H, 6·2. $C_{15}H_{17}O_2NS$ requires C, 65·4; H, 6·2%).

Chlorination of Toluene-p-sulphonyl-2 : 3 : 1-xylidine.—(*a*) By passage of chlorine (1 mol.) into a solution of the sulphonamide in chloroform there was obtained an almost quantitative yield of *4-chloro-N-toluene-p-sulphonyl-2 : 3 : 1-xylidine*, which crystallised from ethanol in large prisms, m. p. 142° (Found: Cl, 11·5. $C_{15}H_{16}O_2NSCl$ requires Cl, 11·5%). This was alternatively prepared from 4-chloro-2 : 3 : 1-xylidine (Hinkel, Collins, and Ayling, *J.*, 1923, **123**, 2972) by interaction with toluene-*p*-sulphonyl chloride in pyridine; it was unchanged after 2 days in concentrated sulphuric acid.

(*b*) Excess of sulphuryl chloride was added to the amide and after the vigorous reaction the excess was removed and the residue dissolved in acetic acid. The small first crop, m. p. 169—172°, recrystallised from acetic acid, gave *4 : 6-dichloro-N-toluene-p-sulphonyl-2 : 3 : 1-xylidine* (XIV) as needles, m. p. 174° (Found: Cl, 21·2. $C_{15}H_{15}O_2NSCl_2$ requires Cl, 20·7%).

The main crop after recrystallisation formed rosettes, m. p. 128—130° (Found: Cl, 33·9. $C_{15}H_{15}O_3NSCl_4$ requires Cl, 34·2%), regarded as 3 : 3 : 4 : 5-*tetrachloro*-1 : 2-*dimethyl*-6-*toluene*-p-*sulphonimido*cyclo*hexene* (XI), for by boiling in ethanolic solution for 3 hr., by dissolution in pyridine, or at 190° it gave 4 : 5 : 6-*trichloro*-N-*toluene*-p-*sulphonyl*-2 : 3 : 1-*xylidine* (XIII), which crystallised from acetic acid in needles, m. p. 206° (Found: Cl, 28·1. $C_{15}H_{14}O_2NSCl_3$ requires Cl, 28·2%). On reduction in acetic acid with zinc dust it gave 4-chloro-*N*-toluene-*p*-sulphonyl-2 : 3 : 1-xylidine (above), and with aniline it reacted briskly to give 4-*anilino*-5 : 6-*dichloro*-N-*toluene*-p-*sulphonyl*-2 : 3 : 1-*xylidine* (XII), which crystallised from acetic acid in prisms, m. p. 205° (Found: C, 57·2; H, 4·2; Cl, 16·3. $C_{21}H_{16}O_2N_2SCl_2$ requires C, 57·9; H, 4·6; Cl, 16·3%).

Chlorination of Toluene-p-*sulphonyl*-3 : 4 : 1-*xylidine*.—(*a*) Chlorine (2 mols.) was passed into the sulphonamide dissolved in chloroform, and the solution then concentrated and diluted with light petroleum. The small crop consisted of toluene-*p*-sulphonamide; the remainder of the material had been converted into an oil.

(*b*) The sulphonamide (5 g.) was treated in the usual way with sulphuryl chloride. The residual oil was very soluble in acetic acid, ethanol, and chloroform, but the solution in the last slowly deposited crystals (0·6 g.), which after two recrystallisations from acetic acid formed needles, m. p. 187° (decomp.) (Found: C, 40·5; H, 2·8; Cl, 38·5. $C_{15}H_{14}O_2NSCl_5$ requires C, 40·0; H, 3·1; Cl, 39·5%). This compound is probably 3 : 3 : 5 : 5 : 6-*pentachloro*-4-*toluene*-p-*sulphonimido*-1 : 2-*dimethyl*cyclo*hexene* (XV), since *N*-acetyl-3 : 4 : 1-xylidine is known to be chlorinated in the 2 : 6-positions (Crossley, *J.*, 1904, **85**, 277). It yielded uncrystallisable material on thermal decomposition, and on reduction with zinc in acetic acid a complex mixture.

Chlorination of N-*Acetyl*-3 : 4 : 1-*xylidine* (method of Crossley, *loc. cit.*).—The mother-liquor remaining after removal of the main crop, on slight dilution, gave a sticky precipitate, which after repeated recrystallisation from acetic acid gave a *monochloro*-derivative in needles, m. p. 153° (Found: Cl, 18·5. $C_{10}H_{12}ONCl$ requires Cl, 18·0%).

Passage of excess of chlorine into a chloroform solution of acetyl-3 : 4 : 1-xylidine led to oils.

Toluene-p-*sulphonyl*-2 : 4 : 1-*xylidine*, obtained by the interaction of 2 : 4 : 1-xylidine with toluene-*p*-sulphonyl chloride in pyridine, crystallised from ethanol in prisms, m. p. 109° (Found: C, 65·4; H, 6·2. $C_{15}H_{17}O_2NS$ requires C, 65·4; H, 6·2%).

Chlorination of Toluene-p-*sulphonyl*-2 : 4 : 1-*xylidine*.—(*a*) Excess of sulphuryl chloride was added to the amide and the residue, after removal of excess of reagent, dissolved in acetic acid. No crystallisation occurred, so the product was precipitated with water and dissolved in ethanol. On cooling, a small crop was obtained, which after recrystallisation from acetic acid formed prisms, m. p. 163° (decomp.) (yield 0·2 g. from 4 g.). This *trichloro-compound* (Found: Cl, 28·4. $C_{15}H_{14}O_2NSCl_3$ requires Cl, 28·2%) may be (XVI) as it contains reactive chlorine, shown by very vigorous reaction with pyridine.

(*b*) Chlorine (2 mols.) was passed into the sulphonamide dissolved in chloroform, and the solution concentrated and diluted with light petroleum. First a very small crop of the compound described under (*a*) was obtained and then a small crop of 3 : 5 : 6-*trichloro*-N-*toluene*-p-*sulphonyl*-2 : 4 : 1-*xylidine* (XVII), which formed needles, m. p. 152°, after recrystallisation from acetic acid (Found: Cl, 28·4%).

(*c*) Commercial sodium hypochlorite solution (20 c.c.) was added to the sulphonamide (5 g.) in acetic acid (50 c.c.) at 50°. The crop obtained on cooling was treated with warm dilute hydrochloric acid, filtered, and repeatedly recrystallised from acetic acid. 6-*Chloro*-N-*toluene*-p-*sulphonyl*-2 : 4 : 1-*xylidine* was obtained in needles, m. p. 158° (Found: C, 57·7; H, 4·9. $C_{15}H_{16}O_2NSCl$ requires C, 58·2; H, 5·2%).

Chlorination of Benzenesulphonyl-2 : 4 : 1-*xylidine*.—(*a*) The amide (8 g.) with sulphuryl chloride gave a viscous mass which was dissolved in benzene. The solution slowly deposited crystals (1·9 g.), m. p. *ca.* 160°, and the mother-liquor on dilution with light petroleum deposited a thick oil of camphory odour. Recrystallisation of the crop from ethanol, acetic acid, or chloroform gave crystals of rather indefinite m. p., the highest being 198—202°. A highly crystalline crop, m. p. 190—193°, was essentially a *trichloro-derivative* (Found: C, 47·5; H, 3·5. $C_{15}H_{14}O_2NSCl_3$ requires C, 47·5; H, 3·7%).

(*b*) Chlorination of the sulphonamide in chloroform led to a similar result.

Chlorination of Toluene-p-*sulphonyl*-2 : 5 : 1-*xylidine*.—(*a*) The sulphonamide was dissolved in sulphuryl chloride, and the oil remaining after removal of excess of reagent was dissolved in acetic acid. The crop, A, m. p. *ca.* 125° (1·5 g. from 4 g.), was filtered off and the filtrate treated with water. The sticky mass remaining after decantation of the aqueous layer was repeatedly recrystallised from ethanol and gave pale yellow needles, m. p. 152° (Found: C, 43·4; H, 3·6;

Cl, 34·0. $C_{15}H_{13}O_2NSCl_4$ requires C, 43·6; H, 3·2; Cl, 34·4%). This *tetrachloro-derivative* is probably (XIX), for on reduction by zinc dust in acetic acid it gave **4**-*chloro*-N-*toluene*-p-*sulphonyl*-**2 : 5 : 1**-*xylidine*, which crystallised from ethanol in plates, m. p. 145° (Found : C, 57·6; H, 4·9. $C_{15}H_{14}O_2NSCl$ requires C, 58·2; H, 5·2%); its vigorous reaction with pyridine gave no recognisable compound; in cold concentrated sulphuric acid it dissolved with evolution of hydrogen chloride, and the solution on precipitation gave a brown resin. The main crop (A) after recrystallisation from acetic acid gave prisms, m. p. 132° (Found : C, 47·6; H, 4·1; Cl, 28·0. $C_{15}H_{14}O_2NSCl_3$ requires C, 47·5; H, 3·7; Cl, 28·2%), regarded as **3 : 3 : 5**-*trichloro*-**6**-*toluene*-p-*sulphonimido*-**1 : 4**-*dimethyl*cyclo*hexa*-**1 : 4**-*diene* (XVIII), for on solution in hot ethanol it was immediately transformed into **3 : 4 : 6**-*trichloro*-N-*toluene*-p-*sulphonyl*-**2 : 5 : 1**-*xylidine* (XX), needles, m. p. 167° (from ethanol) (Found : C, 48·0; H, 3·6; Cl, 27·9%); the same compound was obtained in small yield from the products of thermal decomposition (bath at 160°), and also on suspension in cold sulphuric acid although here the majority of the compound underwent complete decomposition with free evolution of hydrogen chloride. On addition of the diene (XVIII) to pyridine there was produced momentarily a bright yellow colour which faded as the compound dissolved with evolution of considerable heat. On addition of dilute hydrochloric acid there was precipitated **4 : 6**-*dichloro*-N-*toluene*-p-*sulphonyl*-**2 : 5 : 1**-*xylidine*, which crystallised from ethanol in prisms, m. p. 125—126° (Found : C, 52·0; H, 4·3. $C_{15}H_{15}O_2NSCl_2$ requires C, 52·3; H, 4·4%), and was hydrolysed by solution in cold sulphuric acid to the dichloro-base, needles, m. p. 45—48° (from aqueous methanol). This without further purification was acetylated by dissolution in warm acetic anhydride and gave *N*-acetyl-**4 : 6**-dichloro-**2 : 5 : 1**-xylidine, needles, m. p. 166—168° (from ethanol) (Wheeler and Morse, *J. Amer. Chem. Soc.*, 1924, **46**, 2573, give m. p. 167°), and was alternatively prepared by dissolution of acetyl-**2 : 5 : 1**-xylidine in sulphuryl chloride. It was only partly converted into the dichloro-base by several hours' boiling with ethanol–hydrochloric acid. By reduction of the diene (XVIII) in boiling acetic acid with zinc dust there was produced material which crystallised from ethanol in needles, m. p. 117—120°, unchanged after reprecipitation from pyridine (Found : Cl, 20·3%). This appears to be a mixture of mono- and tri-chloro-derivatives, for after dissolution in sulphuric acid, precipitation with water, and recrystallisation from ethanol it yielded pure **4**-chloro-*N*-toluene-*p*-sulphonyl-**2 : 5 : 1**-xylidine, m. p. 145° (above).

3 : 4 : 6-Trichloro-*N*-toluene-*p*-sulphonyl-**2 : 5 : 1**-xylidine was unchanged after treatment in boiling acetic acid with zinc dust, but on dissolution in sulphuric acid readily gave the amine, which formed needles, m. p. 206°, from ethanol (Bureš and Rubeš, *Č. čsl. Lékárn.*, 1928, **8**, 258, give m. p. 206°).

(*b*) Addition of sulphuryl chloride (1 mol.) to the sulphonamide, dissolved in chloroform, gave an almost theoretical yield of **4**-chloro-*N*-toluene-*p*-sulphonyl-**2 : 5 : 1**-xylidine. The same compound was produced but in slightly diminished yield by use of 2 mols. of sulphuryl chloride.

(*c*) Chlorine (2 mols.) was passed into a solution of the sulphonamide (5 g.) in chloroform, and the solution concentrated and diluted with light petroleum. After 24 hr. the first crop (1·2 g.) was collected, and recrystallised from acetic acid and then three times from ethanol to give **4**-chloro-*N*-toluene-*p*-sulphonyl-**2 : 5 : 1**-xylidine. The second crop was recrystallised from acetic acid, to give the trichloro-compound, m. p. 132° (XVIII) (1 g.).

(*d*) Excess of commercial sodium hypochlorite solution was added to the sulphonamide (2 g.) in acetic acid (20 c.c.) at 50°. The crop which separated on cooling was the **4**-chloro-derivative contaminated by difficultly removable unchanged material.

Chlorination of Toluene-p-*sulphonyl*-**2 : 6 : 1**-*xylidine*.—(*a*) Chlorine (2·2 mols.) was passed into a solution of the sulphonamide (Wepster, *Rec. Trav. chim.*, 1954, **73**, 814) in chloroform, and the solution concentrated and diluted with light petroleum. The crop, after repeated recrystallisation from acetic acid or ethanol, gave the *monochloro-derivative* as prisms, m. p. 158° (Found : C, 58·0; H, 4·9. $C_{15}H_{14}O_2NSCl$ requires C, 58·2; H, 5·2%).

(*b*) The sulphonamide (4 g.) with excess of sulphuryl chloride gave the above monochloro-derivative (1·9 g.) and a thick oil.

Bromination of Acetyl-**3 : 4 : 1**-*xylidine*.—Addition of bromine (2 mols.) in acetic acid to the compound in acetic acid (10 parts) produced a thick yellow paste which had passed completely into solution before the addition was complete. After 24 hr. the mixture was poured into water, and the precipitate washed free from bromine and dried. It had m. p. 155—160° and was essentially *N*-acetyl-**6**-bromo-**3 : 4 : 1**-xylidine free from dibromo-derivative (Found : Br, 33·7. Calc : Br, 33·0%). Recrystallisation from ethanol raised the m. p. to 164° (Mills and Nixon give 164°). Hydrolysis was brought about by ½ hour's heating with an ethanol–concentrated hydrochloric acid (2 : 1). The resultant **6**-bromo-**3 : 4 : 1**-xylidine gave a *toluene*-p-*sulphonyl*

derivative, which crystallised from ethanol in prisms, m. p. 122° (Found: Br, 24·0. $C_{15}H_{16}O_2NSBr$ requires Br, 23·9%).

Bromination of Toluene-p-sulphonyl-3 : 4 : 1-xylidine.—(*a*) Addition of bromine (1 mol.) in chloroform to the compound in chloroform gave the 6-bromo-derivative (above) in almost quantitative yield. Heating in chloroform with bromine (2 mols.) led to the same compound together with a variable amount of the hydrobromide of 2 : 6-dibromo-3 : 4 : 1-xylidine.

(*b*) Addition of bromine (2 mols.) to the sulphonamide in cold pyridine gave in high yield the 2 : 6-*dibromo-derivative*, which formed needles, m. p. 165°, from ethanol (Found: Br, 38·0. $C_{15}H_{15}O_2NSBr_2$ requires Br, 38·7%). By dissolution in cold sulphuric acid this gave the 2 : 6-dibromo-amine (Jaeger and Blanksma, *loc. cit.*), which gave an *acetyl derivative*, m. p. 198° (Found: C, 36·9; H, 3·5. $C_{16}H_{11}ONBr_2$ requires C, 37·4; H, 3·4%). This compound crystallised from ethanol in needles, which in contact with the solvent were slowly transformed into prisms.

Passage of chlorine (1—2 mols.) into either *N*-acetyl-6-bromo- or 6-bromo-*N*-toluene-*p*-sulphonyl-3 : 4 : 1-xylidine in chloroform led to no crystallisable material other than the initial compounds. 6-Bromo-*N*-toluene-*p*-sulphonyl-3 : 4 : 1-xylidine was unchanged after treatment in pyridine solution with iodine.

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*Alicyclic Glycols. Part XIII.** 1 : 2-*Bishydroxymethylcyclopentane.*

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The *cis*- and the *trans*-form of the above glycol have been obtained by reduction of the corresponding stereoisomers of dimethyl *cyclo*pentane-1 : 2-dicarboxylate with lithium aluminium hydride. Syntheses of the intramolecular ethers, *cis*- and *trans*-3-oxa*bicyclo*[3 : 3 : 0]octane, and of the related cyclic sulphides, *cis*- and *trans*-3-thia*bicyclo*[3 : 3 : 0]octane, are described. The *trans*-sulphide is also obtained by a cyclisation which occurs during the partial desulphurisation of *trans*-1 : 2-bismercaptomethyl-*cyclo*pentane. The *trans*-oxide (IX) and the *trans*-sulphide (XIII) are of special interest because of the presence of two mutually *trans*-fused five-membered rings.

The tetrahydrofuran ring in each cyclic oxide is readily broken by reaction with acetyl bromide; the products have been used to synthesise *cis*- and *trans*-2-methyl*cyclo*pentylmethanol.

SYNTHESES of the various bishydroxymethyl*cyclo*hexanes, and their uses in elucidating the configurations of the dimethyl*cyclo*hexanes and the methyl*cyclo*hexylmethanols, were described by Haggis and Owen (*J.*, 1953, 389, 399, 404, 408); later, Birch and Dean (*J.*, 1953, 2477) prepared the 1 : 3-bishydroxymethyl*cyclo*pentanes and converted them into the 1 : 3-dimethyl*cyclo*pentanes, thus establishing the configurations of the latter. When the present work was begun, neither of the 1 : 2-bishydroxymethyl*cyclo*pentanes (I) and (VI) had been described, but each was easily prepared by reduction with lithium aluminium hydride of the appropriate stereoisomer of dimethyl *cyclo*pentane-1 : 2-dicarboxylate (some improvements in the preparation of the 1 : 2-dicarboxylic acid from *cyclo*pentanone are outlined in the experimental section). Subsequently, the *trans*-diol has been described by Halford and Weissmann (*J. Org. Chem.*, 1952, **17**, 1276) and by Bailey and Sorenson (*J. Amer. Chem. Soc.*, 1954, **76**, 5421), though no derivatives were recorded; the physical constants of our product differed considerably from those of the former authors, but agreed with those of the latter. The *cis*- and the *trans*-diol each gave a crystalline toluene-*p*-sulphonate, methanesulphonate, and α-naphthylurethane.

* Part XII, Owen and Saharia, *J.*, 1953, 2582.

Haggis and Owen (*J.*, 1953, 389) described three methods by which the cyclic oxide, octahydro*iso*benzofuran (V), could be obtained from 1 : 2-bishydroxymethyl*cyclo*hexane : (i) by direct dehydration over alumina, or by heating in acid solution; (ii) by alkaline hydrolysis of the dimethanesulphonate; (iii) as a by-product in the preparation of the dimethanesulphonate or ditoluene-*p*-sulphonate. Although the oxide (V) was isolated in the *cis*- and the *trans*-form by use of the corresponding stereoisomer of the diol, it was expected in the present investigation that 3-oxa*bicyclo*[3 : 3 : 0]octane would be obtainable by similar methods only as the *cis*-form (II), since the strain involved in the *trans*-fusion of two five-membered rings rendered the formation of the *trans*-oxide much more doubtful. This view was supported by small-scale comparative experiments with *cis*- and with *trans*-1 : 2-bishydroxymethyl*cyclo*pentane, which showed that only the former was dehydrated to the oxide when heated with alumina or aqueous sulphuric acid. On a preparative scale, reaction of the *cis*-diol with boiling 18% sulphuric acid gave the pure oxide (II) in 76% yield. It was also obtained by hydrolysis of the *cis*-dimethanesulphonate with boiling aqueous potassium hydroxide, although it was then contaminated with a small proportion of an unsaturated compound, probably the isomeric 2-methylene*cyclo*pentylmethanol (IV) since it gave a small amount of formaldehyde on ozonolysis. The cyclic oxide was also formed, together with the *cis*-dimethanesulphonate, when the latter was prepared by slow addition of methanesulphonyl chloride to a solution of the *cis*-diol in pyridine; reversed order in addition gave only traces of the oxide.

Although no cyclic oxide could be prepared by dehydration of the *trans*-diol, alkaline hydrolysis of the *trans*-dimethanesulphonate (VII) unexpectedly gave a 67% yield of pure *trans*-3-oxa*bicyclo*[3 : 3 : 0]octane (IX), the physical constants of which were slightly different from those of the *cis*-isomer. Both compounds had the strong odour characteristic of cyclic oxides; their stereochemical individuality follows from the ring-fission reactions described later. The freedom of the *trans*-oxide from unsaturated material (cf. the *cis*-oxide prepared from the dimethanesulphonate) indicates that the competing elimination reaction is suppressed. This is probably due to the shielding effect of the 1-methanesulphonyloxymethyl group in the ester (VII), which hinders the attack by OH^- on the neighbouring hydrogen atom attached to $C_{(2)}$; in the *cis*-compound (III) the hydrogen atom is not so protected.

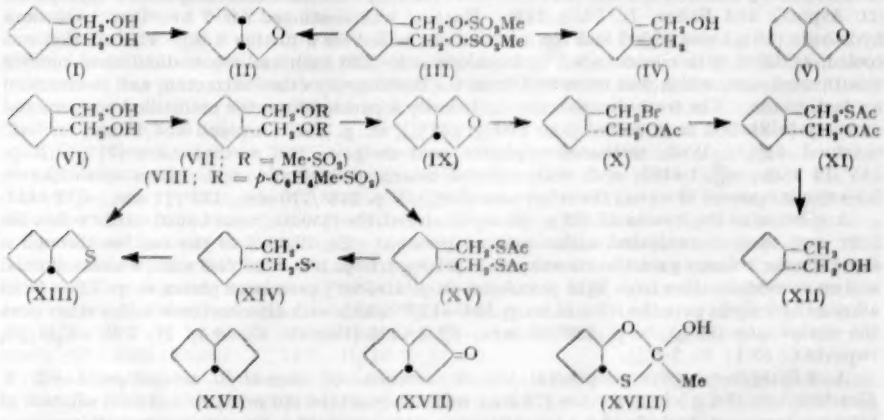
The *trans*-ditoluene-*p*-sulphonate (VIII) reacted smoothly with potassium thiolacetate to give *trans*-1 : 2-bisacetylthio*cyclo*pentane (XV). In the *cyclo*hexane series, conversion of a bisthiolacetate into the corresponding dimethyl*cyclo*hexane was carried out by desulphurisation in methanol with Raney nickel, and with the relatively small amounts of materials available there had been considerable difficulty in isolating the pure hydrocarbon. Even greater difficulty would arise with the more volatile dimethyl*cyclo*pentanes, and some exploratory experiments were therefore carried out involving desulphurisation in the absence of an organic solvent. The bisthiolacetate (XV) was hydrolysed to the dithiol with aqueous sodium hydroxide, and the resulting solution was treated directly with Raney nickel. The result was unexpected; in addition to some hydrocarbon there was formed a volatile crystalline solid, which contained sulphur and was identified as *trans*-3-thia*bicyclo*[3 : 3 : 0]octane (XIII) by synthesis from the *trans*-ditoluene-*p*-sulphonate (VIII) and sodium sulphide. The *cis*-isomer, a liquid, was similarly synthesised from the *cis*-ditoluene-*p*-sulphonate. The infrared spectra of the two sulphides (determined by Mr. R. L. Erskine, Spectrographic Laboratory), although similar in general form, exhibited marked differences in detail, and showed each isomer to be free from the other. Each sulphide on oxidation with hydrogen peroxide gave a different crystalline sulphone.

Desulphurisation with Raney nickel is probably a free-radical reaction (Hauptmann and Wladislaw, *J. Amer. Chem. Soc.*, 1950, **72**, 707, 711; Bonner, *ibid.*, 1952, **74**, 1034; Birch and Dean, *Annalen*, 1954, **585**, 234) and the formation of the sulphide (XIII) can clearly occur through the intermediate diradical (XIV); the isolation of the sulphide (XIII) under the above conditions is undoubtedly due to its insolubility in the aqueous reaction medium, which retards its further desulphurisation to the hydrocarbon.

Compounds containing two *trans*-fused five-membered rings are very rare. The only well-authenticated homocyclic examples are *trans-bicyclo*[3 : 3 : 0]octane (XVI) and the

β-ketone (XVII) from which it was derived by reduction (Barrett and Linstead, *J.*, 1935, 436, 1069); the structure of a steroid derivative considered to contain the system (XVI) (Wendler, Hirshmann, Slates, and Walker, *Chem. and Ind.*, 1954, 901) is based only on the probable stereochemical course of a pinacolic change. In the heterocyclic field, *allo*biotin and *epiallo*biotin contain the *trans*-2 : 4-diaza-7-thia*bicyclo*[3 : 3 : 0]octane system (Harris, Mozingo, Wolf, Wilson, and Folkers, *J. Amer. Chem. Soc.*, 1945, **67**, 2102); the anhydride of *trans-cyclo*pentane-1 : 2-dicarboxylic acid, which would provide a further example, may not be monomeric (cf. Bredt, *Annalen*, 1924, **437**, 9). In view of the fact that the ketone (XVII) could not be prepared by Dieckmann cyclisation of diethyl *trans-cyclo*pentane-1 : 2-diacetate but only by the more vigorous method of heating the *trans*-acid with barium hydroxide at 320—350°, it is all the more surprising that the ring-closures leading to the *trans*-oxide (IX) and the *trans*-sulphide (XIII) should occur under such comparatively mild conditions. Also significant in this connection is the extreme ease with which *trans*-2-acetylthio*cyclo*pentanol is isomerised to 2-mercapto*cyclo*pentyl acetate by cold dilute alkali (Harding and Owen, *J.*, 1954, 1528), because if this acetyl migration follows the usual mechanism it must involve the formation of the intermediate *trans*-fused orthoacetate (XVIII). These results clearly indicate that the *trans*-fused compounds are formed much more readily than would be expected on conventional stereochemical grounds.

Fission of the tetrahydrofuran ring in the *trans*-oxide (IX) with acetyl bromide gave *trans*-2-bromomethyl*cyclo*pentylmethyl acetate (X), the configuration of which was confirmed by its conversion into *trans*-1 : 2-bisacetoxymethyl*cyclo*pentane, followed by hydrolysis to the *trans*-diol (VI), identified as the ditoluene-*p*-sulphonate. Reaction of the acetate bromide (X) with potassium thiolacetate gave *trans*-2-acetylthio*cyclo*pentylmethyl acetate (XI), which after desulphurisation and hydrolysis furnished *trans*-2-methyl*cyclo*pentylmethanol (XII). A similar series of reactions, starting from the *cis*-oxide, gave the *cis*-isomer of (XII). Both alcohols were liquids, the physical properties of which were in accordance with the Auwers–Skita rules; the *cis*- and the *trans*-3 : 5-dinitrobenzoate, the *cis*- and the *trans*-α-naphthylurethane, and the *cis*-phenylurethane were obtained crystalline. Anziani and Cornubert (*Bull. Soc. chim.*, 1948, 857) obtained a



by-product from the interaction of *cis*-2-methyl*cyclo*hexylamine and nitrous acid, which they suggested might be one of the 2-methyl*cyclo*pentylmethanols, but the structure was not established. Nenitzescu and Vantu (*Bull. Soc. chim. France*, 1935, **2**, 2209), by reduction of ethyl 2-methyl*cyclo*pentanecarboxylate with sodium and alcohol, prepared a 2-methyl*cyclo*pentylmethanol of undetermined configuration (no crystalline derivatives were described). The physical constants indicate that their product was probably mainly the *trans*-form, as would be expected on stereochemical grounds, this being less hindered than the *cis*-isomer. This conclusion is supported by a comparison of the properties of their

1 : 2-dimethyl*cyclo*pentane (obtained by reduction of the bromide derived from the alcohol) with those of the pure stereoisomers described by Forziati and Rossini (*J. Res. Nat. Bur. Stand.*, 1949, **43**, 473).

Very recently, Pines and Hoffman (*J. Amer. Chem. Soc.*, 1954, **76**, 4417) have obtained *trans*-2-methyl*cyclo*pentylmethanol from *trans*-2-methyl*cyclo*pentanecarboxylic acid, the assignment of configuration being based on the conversion of the alcohol, through its toluene-*p*-sulphonate, into *trans*-1 : 2-dimethyl*cyclo*pentane. Our stereospecific synthesis of the alcohol, taken in conjunction with the latter correlation, provides an independent chemical proof of the configurations of the 1 : 2-dimethyl*cyclo*pentanes, hitherto founded only on physical data.

Experimental

*cyclo*Pentanone cyanohydrin was prepared from the ketone and liquid hydrogen cyanide, catalysed by the addition of a few drops of 60% aqueous potassium hydroxide, by Cook and Linstead's method (*J.*, 1934, 959), except that the mixture was kept at 0° for 14 hr. Distillation of the acidified product gave the hydroxy-nitrile, b. p. 122°/21 mm., n_D^{20} 1·4562, in 91% yield. The hydroxy-acid, obtained by hydrolysis (Meerwein and Unkel, *Annalen*, 1910, **376**, 152), gave ethyl 1-hydroxy*cyclo*pentanecarboxylate, b. p. 88°/15 mm., n_D^{16} 1·4510, in 80% yield by esterification with ethanol and sulphuric acid in benzene, with azeotropic removal of the water formed (cf. Cook and Linstead, *loc. cit.*).

Dehydration of *cyclo*pentanone cyanohydrin with thionyl chloride by Bauer and Cymerman's method (*J.*, 1950, 1826) gave 1-cyano*cyclo*pentene, b. p. 76—78°/39 mm., n_D^{17} 1·4730, in 84% yield, though the product always contained traces of halogen and sulphur (Found: S, 0·8%). With ethanol–sulphuric acid (Cook and Linstead, *loc. cit.*) it gave ethyl *cyclo*pent-1-enecarboxylate, b. p. 81—83°/20 mm., n_D^{20} 1·4598; this was also obtained by dehydration of ethyl 1-hydroxy*cyclo*pentanecarboxylate with phosphorus pentachloride (Cook and Linstead, *loc. cit.*), but the product, b. p. 87—89°/21 mm., n_D^{17} 1·4582, contained traces of halogen, and although the latter could be removed by heating with diethylaniline the yield of pure unsaturated ester was then low.

cyclo*Pentane*-1 : 2-*dicarboxylic Esters*.—To a boiling, stirred solution of potassium cyanide (15 g.) in water (30 c.c.), under reflux, ethyl *cyclo*pent-1-enecarboxylate (54·5 g.) in ethanol (200 c.c.) and potassium cyanide (25 g.) in water (50 c.c.) were simultaneously added during 1 hr. (cf. Aspinall and Baker, *J.*, 1950, 743). Heating was continued for 7 hr., then potassium hydroxide (36 g.) was added and the mixture was boiled for a further 6 hr. The solution was cooled, acidified with concentrated hydrochloric acid (120 c.c.), and steam-distilled to remove unsaturated acid, which was recovered from the distillate by ether-extraction and re-esterified for further use. The *trans*-dicarboxylic acid slowly separated from the undistilled portion, and on recrystallisation from water gave 37·5 g. (61%), m. p. 161° (Aspinall and Baker, *loc. cit.*, obtained 44%). With methanol–sulphuric acid it gave the methyl ester (77%), b. p. 115°/12 mm., n_D^{20} 1·4491, and with ethanol–toluene-*p*-sulphonic acid–carbon tetrachloride (azeotropic removal of water) the ethyl ester (86%), b. p. 248°/770 mm., 133°/17 mm., n_D^{18} 1·4451.

A solution of the *trans*-acid (22 g.) in acetic anhydride (250 c.c.) was boiled under reflux for 3 hr. and then concentrated under reduced pressure. Distillation of the residue through a short Fenske column gave the *cis*-anhydride (11·8 g.), b. p. 100—102°/1·5 mm., which solidified and on recrystallisation from light petroleum (b. p. 40—80°) gave large plates, m. p. 72°. Brief alkaline hydrolysis gave the *cis*-acid, m. p. 134—135°, which with diazomethane in dry ether gave the *methyl ester* (96%), b. p. 129°/20 mm., n_D^{21} 1·4528 (Found: C, 58·4; H, 7·75. $C_9H_{14}O_4$ requires C, 58·1; H, 7·6%).

1 : 2-*Bishydroxymethyl*cyclo*pentane*.—(i) A solution of dimethyl *cis-cyclo*pentane-1 : 2-dicarboxylate (7·7 g.) in dry ether (75 c.c.) was slowly added (20 min.) to a stirred solution of lithium aluminium hydride (2·6 g.) in dry ether (150 c.c.) at 0°. Stirring was maintained for a further hour at 0°, water and 10% sulphuric acid were then cautiously added until no solid remained, and the ether layer was removed; the aqueous portion was continuously extracted with ether for 24 hr. Evaporation of the dried (K_2CO_3) extracts and distillation of the residue gave cis-1 : 2-*bishydroxymethyl*cyclo*pentane* (5·1 g., 95%), b. p. 103°/0·15 mm., n_D^{21} 1·4840 (Found: C, 64·7; H, 10·9. $C_7H_{14}O_2$ requires C, 64·6; H, 10·8%).

(ii) Similar reductions of the *trans*-dimethyl and the *trans*-diethyl esters gave the *trans*-diol, b. p. 147°/11 mm., 100°/0·02 mm., n_D^{22} 1·4760 (Found: C, 64·5; H, 10·8%). Halford and Weissmann (*loc. cit.*) give b. p. 117—118°/0·6 mm., n_D^{25} 1·4480. Bailey and Sorenson (*loc. cit.*) give b. p. 127—129°/2·4 mm., n_D^{25} 1·4771.

Derivatives of the cis-*Diol.*—The *cis*-diol (1 g.) and toluene-*p*-sulphonyl chloride (4·5 g.) in pyridine (10 c.c.) at 0° gave the cis-*ditoluene*-p-*sulphonate* (2·5 g.), which crystallised from methanol in fluffy needles, m. p. 82° (Found: C, 57·75; H, 6·4; S, 14·4. $C_{21}H_{24}O_6S_2$ requires C, 57·5; H, 6·0; S, 14·6%).

Addition of a solution of the *cis*-diol (9·7 g.) in pyridine (40 c.c.) to methanesulphonyl chloride (21 g.) in pyridine (60 c.c.) gave in the same way the cis-*dimethanesulphonate* (18·7 g.), m. p. 59° (from aqueous methanol) (Found: C, 37·9; H, 6·4; S, 22·0. $C_9H_{18}O_6S_2$ requires C, 37·8; H, 6·4; S, 22·4%). Reversed addition of the reagents gave a much lower yield of the derivative, accompanied by the cyclic oxide (see below).

Reaction of the *cis*-diol (0·15 g.) with α-naphthyl *iso*cyanate (0·46 g.) for 1 hr. at 100° gave the cis-*bis*-α-*naphthylurethane*, m. p. 149° (from aqueous ethanol) (Found: C, 73·8; H, 6·3; N, 6·1. $C_{29}H_{24}O_4N_2$ requires C, 74·3; H, 6·0; N, 6·0%).

Derivatives of the trans-*Diol.*—By the methods used for the *cis*-derivatives there were obtained the trans-*ditoluene*-p-*sulphonate* (87%), thick needles (from methanol), m. p. 64° (Found: C, 57·6; H, 6·2; S, 14·3%); the trans-*dimethanesulphonate* (85%), needles (from methanol), m. p. 60° (Found: C, 38·05; H, 6·5; S, 22·5%), depressed to 52—54° on admixture with the *cis*-isomer; and the trans-*bis*-α-*naphthylurethane* (40%), m. p. 155° [from benzene–petroleum (b. p. 60—80°)] (Found: C, 74·5; H, 6·2; N, 5·9%).

trans-1 : 2-*Di*(*acetylthiomethyl*)cyclo*pentane.*—The *trans*-ditoluene-*p*-sulphonate (6 g.), potassium thiolacetate (4·7 g.), thiolacetic acid (0·1 c.c.), and ethanol (60 c.c.) were boiled together under reflux for 4 hr. The solvent was then removed under reduced pressure and the residue was shaken with water and chloroform. The chloroform solution was washed, dried, and concentrated; distillation of the residue gave the trans-*bisthiolacetate* (2·9 g., 86%), b. p. 116—118°/0·05 mm., n_D^{21} 1·5297 (Found: C, 53·7; H, 7·3; S, 26·1. $C_{11}H_{18}O_2S_2$ requires C, 53·65; H, 7·4; S, 26·0%).

Comparative Dehydrations of the Stereoisomeric 1 : 2-*Bishydroxymethylcyclopentanes.*—(i) A solution of the *cis*-diol (55 mg.) in 18% aqueous sulphuric acid (0·3 c.c.) was kept at 100°. After 5 min. a strong odour of cyclic oxide was present; no unsaturation could be detected even after 4 hours' heating. In an identical experiment with the *trans*-diol, no odour of oxide could be detected; after 4 hr. the solution was unsaturated towards neutral permanganate.

(ii) A mixture of *cis*-diol (40 mg.) and dried alumina (150 mg.) was slowly heated to 210° (oil-bath); a strong odour of the cyclic oxide was evident. No oxide could be detected in a similar experiment with the *trans*-diol.

cis-3-*Oxa*bicyclo[3 : 3 : 0]*octane.*—(i) The *cis*-diol (9·4 g.) and 18% aqueous sulphuric acid (50 c.c.) were boiled together under reflux for 20 min., and the mixture was then distilled until no more oil was present, water being gradually added to the distillation flask to maintain the volume. The distillate was extracted with ether to give an oil, which on distillation furnished cis-3-*oxa*bicyclo[3 : 3 : 0]*octane* (6·15 g., 76%), b. p. 149°, n_D^{20} 1·4590 (Found: C, 74·8; H, 10·8. $C_7H_{12}O$ requires C, 75·0; H, 10·8%); the compound has a characteristic camphoraceous odour.

(ii) Methanesulphonyl chloride (34 g.) was slowly added (1 hr.) to a solution of the *cis*-diol (15·6 g.) in pyridine (85 c.c.) at 0°. The mixture was set aside at 0° overnight and then diluted with ice and water; the precipitated oil partly crystallised. The solid (4·9 g.) was collected, and on recrystallisation gave the *cis*-dimethanesulphonate (4·3 g.), m. p. 59°. The oil was taken up in ether, and the aqueous portion was extracted with ether. The combined extracts were washed successively with dilute sulphuric acid, aqueous sodium hydrogen carbonate, and water, and were dried (Na_2SO_4) and evaporated. Distillation of the residue gave a fraction (1·5 g.), b. p. 60—80°/20 mm., which on redistillation over sodium gave the *cis*-oxide, n_D^{26} 1·4600 (Found: C, 74·7; H, 10·6%).

(iii) A suspension of the *cis*-dimethanesulphonate (17 g.) in 15% aqueous potassium hydroxide (180 c.c.) was vigorously boiled under reflux for 2 hr. The condenser was then rearranged for distillation, and boiling was continued until no more oil was collected in the distillate. The latter was extracted with ether, and distillation of the product gave fractions (4·9 g., 74%), b. p. 152—167°, n_D^{18} 1·4623—1·4772, which, although containing much *cis*-oxide (odour), were unsaturated to bromine water. A portion (0·1 g.) of the highest-boiling fraction was ozonised in ethyl acetate (3 c.c.), the exit gases being passed through water; this solution, together with the distillate obtained by steam-distillation of the ozonolysis product, on treatment with dimedone gave the formaldehyde derivative (9 mg.), m. p. and mixed m. p. 188°. The usual 30—35% recovery of formaldehyde from a $\cdot CH_2$ group being assumed, the yield corresponds to the presence of *ca.* 10% of 2-methylene*cyclo*pentylmethanol.

trans-3-*Oxa*bicyclo[3 : 3 : 0]*octane.*—Reaction of the *trans*-dimethanesulphonate (10·5 g.)

with boiling 18% aqueous potassium hydroxide (70 c.c.) for 1½ hr., followed by working-up as described for the similar reaction with the *cis*-isomer, gave trans-3-*oxa*bicyclo[3 : 3 : 0]*octane* (2·75 g., 67%), b. p. 158°, n_D^{23} 1·4631 (Found: C, 74·7; H, 10·9%). The product was free from unsaturated material; it had a strong odour, similar to that of the *cis*-compound.

cis-3-*Thia*bicyclo[3 : 3 : 0]*octane*.—A solution of sodium sulphide nonahydrate (3 g.) in water (4 c.c.) was added to a solution of the *cis*-ditoluene-*p*-sulphonate (1·95 g.) in hot ethanol (5 c.c.). The mixture was boiled under reflux for 30 min., then diluted with water (20 c.c.) and distilled, more water being added as required. The first portion of the distillate, mainly alcoholic, was clear, and was reserved. The distillate then became cloudy, and it was collected until it became clear again; extraction of this aqueous fraction with ether, followed by evaporation of the washed and dried (K_2CO_3) extracts, and distillation of the residue, gave cis-3-*thia*bicyclo[3 : 3 : 0]*octane* as a colourless oil (0·25 g.), b. p. 180—184°, n_D^{21} 1·5218 (Found: C, 65·6; H, 9·7; S, 25·0. $C_7H_{12}S$ requires C, 65·6; H, 9·4; S, 25·0%), with a powerful and characteristically sulphurous odour.

To the alcoholic portion of the original distillate, a warm saturated solution of mercuric chloride in ethanol was added until no more solid was precipitated. The *adduct* was collected, washed with ethanol, and recrystallised from ethanol to give white felted needles (0·81 g.), m. p. 163—164° (Found: C, 21·3; H, 3·3; S, 7·3; Cl, 17·4. $C_7H_{12}S,HgCl_2$ requires C, 21·0; H, 3·0; S, 8·0; Cl, 17·7%).

Oxidation of the cyclic sulphide (0·15 g.) in acetic acid (0·5 c.c.) by the addition of 30% hydrogen peroxide (0·5 c.c.) was exothermic. The hot solution was evaporated on the steam-bath to a solid residue, which on recrystallisation from water gave the cis-*sulphone* as long needles, m. p. 70° (Found: C, 52·2; H, 7·7; S, 19·6. $C_7H_{12}O_2S$ requires C, 52·5; H, 7·55; S, 20·0%).

trans-3-*Thia*bicyclo[3 : 3 : 0]*octane*.—(i) Reaction of the *trans*-ditoluene-*p*-sulphonate (1·8 g.) in ethanol (10 c.c.) with sodium sulphide nonahydrate (3 g.) in water (4 c.c.) was carried out as for the *cis*-compound. The cloudy aqueous portion of the distillate on extraction gave trans-3-*thia*bicyclo[3 : 3 : 0]*octane* (0·3 g.), b. p. 190—195°, which solidified in colourless needles, m. p. 29°, n_D^{21} 1·5233 (Found: C, 66·0; H, 9·5; S, 24·5%), somewhat volatile at room temperature, and possessing an odour similar to that of the *cis*-isomer.

The alcoholic portion of the original distillate gave the mercuric chloride adduct, long white needles, m. p. 181—182° (from ethanol) (Found: C, 21·4; H, 3·2; S, 8·0%).

Oxidation of the cyclic sulphide with hydrogen peroxide gave the trans-*sulphone*, fine needles, m. p. 120° (from water) (Found: C, 52·1; H, 7·5; S, 19·6%).

(ii) *trans*-1 : 2-Bisacetylthio*cyclo*pentane (5·9 g.), sodium hydroxide (5 g.), and water (25 c.c.) were stirred at 75° for 4 hr. under nitrogen. More alkali (5 g.) in water (10 c.c.) was added, and the mixture was boiled under reflux for 4 hr.; it was then homogeneous. Moist Raney nickel (*ca.* 30 g.) was added in small portions during 5 hr. at 75°; no free thiol could then be detected. The solution was then slowly distilled; considerable difficulty was experienced owing to frothing, and it was necessary to redistil the distillate. The first fraction (*ca.* 5 c.c.), containing oily drops in suspension, was saturated with potassium carbonate, and the upper layer was removed, dried (Na), and distilled to give (i) (probably) crude *trans*-1 : 2-dimethyl*cyclo*pentane (50 mg.), b. p. up to 98°, n_D^{20} 1·4185 (last drop, n_D^{20} 1·4240), which had a slight odour of the cyclic sulphide, and (ii) a less volatile oil, having a powerful odour of cyclic sulphide, which crystallised in the side-arm and had m. p. 28°, not depressed on admixture with the synthetic *trans*-sulphide.

Further distillation of the aqueous solution gave fractions which were cloudy and odorous; when stored at 0° they deposited needles which were collected and converted into the mercuric chloride adduct, m. p. 178° (Found: C, 21·3; H, 3·3; S, 7·95%). Repeated recrystallisation failed to raise the m. p. to that of the synthetic *trans*-compound, though the crystalline form was similar to that of the latter, and quite distinct from that of the *cis*-adduct.

Infrared Spectra.—Copies of the spectra of the *cis*- and the *trans*-sulphide have been deposited with the Chemical Society. Photocopies (prince 3*s*. 0*d*. each) may be obtained from the General Secretary on application, quoting C.S. nos. 213 (*cis*) or 214 (*trans*).

2-*Bromomethyl*cyclo*pentylmethyl Acetate*.—(i) Freshly distilled acetyl bromide (8·4 g.) was added to *cis*-3-*oxabicyclo*[3 : 3 : 0]octane (6·3 g.; prepared by the method of direct dehydration); there was only a slow rise in temperature, and the mixture was therefore heated at 100° for 25 min. The liquid, which had become pale brown, was cooled, poured into ice-water, and extracted with chloroform. Evaporation of the washed (aqueous sodium hydrogen carbonate) and dried (Na_2SO_4) extracts, and distillation of the residue gave cis-2-*bromomethyl*cyclo*pentylmethyl acetate* as a colourless oil (11·6 g., 88%), b. p. 96°/1 mm., n_D^{20} 1·4899 (Found: C, 45·95; H, 6·6; Br, 33·3. $C_9H_{15}O_2Br$ requires C, 46·0; H, 6·4; Br, 34·0%). Use of a slightly impure

cyclic oxide (prepared from the *cis*-dimethanesulphonate) resulted in a vigorous reaction on addition to the acetyl bromide, and the product obtained, b. p. 96—98°/2 mm., n_D^{22} 1·4900, was not quite pure (Found: C, 45·6; H, 6·7; Br, 36·1%).

(ii) A similar reaction between the *trans*-oxide (3·5 g.) and acetyl bromide (4·3 g.) gave trans-2-*bromomethylcyclopentylmethyl acetate* (4·8 g., 65%), b. p. 98°/1·5 mm., n_D^{18} 1·4861 (Found: C, 45·9; H, 6·6; Br, 34·15%).

1 : 2-*Bisacetoxymethylcyclopentane*.—(i) *trans*-2-Bromomethyl*cyclo*pentylmethyl acetate (1·1 g.), fused potassium acetate (2 g.), and dry ethanol (21 c.c.) were boiled together under reflux for 18 hr. The solvent was removed under reduced pressure, and the residue was treated with water and ether. The ethereal extract gave a product which still contained halogen, and the oil was therefore mixed with silver acetate (3 g.) and acetic acid (10 c.c.) and boiled under reflux for 3 hr. Working up as before gave the *trans*-diacetate (0·35 g.), b. p. 104°/1 mm., n_D^{24} 1·4522 (Found: C, 61·3; H, 8·5. Calc. for $C_{11}H_{18}O_4$: C, 61·7; H, 8·45%). Bailey and Sorenson (*loc. cit.*) give b. p. 116°/2 mm., n_D^{25} 1·4471. The product was added to methanolic sodium methoxide (20 c.c., containing 0·1 g. of sodium), and the solution was boiled for 90 min., then neutralised with carbon dioxide and evaporated to dryness. Treatment of the residue with toluene-*p*-sulphonyl chloride and pyridine gave the *trans*-ditoluene-*p*-sulphonate, m. p. and mixed m. p. 64°.

(ii) *cis*-2-Bromomethyl*cyclo*pentylmethyl acetate (1·4 g.) and potassium acetate (3·1 g.), in boiling acetic acid (25 c.c.) for 12 hr., gave a halogen-containing product which was treated further with silver acetate, as described above. The crude *cis*-diacetate (0·4 g.), b. p. 107—111°/2 mm., n_D^{20} 1·4525 (Found: C, 62·5; H, 8·6%), was deacetylated with methanolic sodium methoxide and the diol characterised as the *cis*-ditoluene-*p*-sulphonate, which after purification by chromatography on magnesium trisilicate had m. p. 78—79°, mixed m. p. 80°; the yield was very poor.

2-*Acetylthiomethylcyclopentylmethyl Acetate*.—(i) A solution of *cis*-2-bromomethyl*cyclo*pentylmethyl acetate (9·0 g.), potassium thiolacetate (9·0 g.), and thiolacetic acid (0·1 g.) in ethanol (90 c.c.) was boiled under reflux for 30 min. under nitrogen. The product still contained halogen, and was combined with that from a similar reaction (on 3·5 g. of bromide acetate) and treated for 2 hr. with potassium thiolacetate (5 g.) in boiling ethanol (75 c.c.). The solvent was removed under reduced pressure, and the residue was shaken with water and extracted with chloroform to give cis-2-*acetylthiomethylcyclopentylmethyl acetate* (10·2 g.), b. p. 92—94°/0·0003 mm., n_D^{18} 1·5012 (Found: C, 57·2; H, 8·0; S, 13·6. $C_{11}H_{18}O_3S$ requires C, 57·4; H, 7·9; S, 13·9%).

(ii) Reaction of *trans*-2-bromomethyl*cyclo*pentylmethyl acetate (4·6 g.) with potassium thiolacetate (3·0 g.) and thiolacetic acid (0·1 c.c.) in boiling ethanol for 1½ hr. gave, when worked up as above, trans-2-*acetylthiomethylcyclopentylmethyl acetate* (3·85 g., 85%), b. p. 129°/1 mm., n_D^{22} 1·4902 (Found: C, 57·4; H, 8·2; S, 13·65%).

2-*Methylcyclopentylmethanol*.—(i) Freshly prepared Raney nickel (*ca.* 30 g.) was added in portions to a boiling solution of *cis*-2-acetylthiomethyl*cyclo*pentylmethyl acetate (7·4 g.) in boiling ethanol (100 c.c.). After 5 hr. no thiol or thiolacetate could be detected, and the solution was filtered. Sodium hydroxide (2·5 g.) was added, and the solution was boiled for 2 hr. and then concentrated to small bulk. The residue was diluted with water and extracted with ether to give cis-2-*methylcyclopentylmethanol* (2·2 g.), b. p. 114°/78 mm., n_D^{17} 1·4632 (Found: C, 73·6; H, 12·0. $C_7H_{14}O$ requires C, 73·6; H, 12·35%). The 3 : 5-*dinitrobenzoate* crystallised from methanol in flakes, m. p. 66—67° (Found: C, 54·7; H, 5·2; N, 9·3. $C_{14}H_{16}O_6N_2$ requires C, 54·55; H, 5·2; N, 9·1%); the *phenylurethane* formed felted needles, m. p. 64°, from light petroleum (b. p. 40—60°) (Found: C, 72·2; H, 8·0; N, 6·3. $C_{14}H_{19}O_2N$ requires C, 72·1; H, 8·2; N, 6·0%); and the *α-naphthylurethane*, needles, m. p. 92° [from light petroleum (b. p. 60—80°)] (Found: C, 76·6; H, 7·6; N, 5·1. $C_{18}H_{21}O_2N$ requires C, 76·3; H, 7·5; N, 4·9%).

(ii) Similar treatment of *trans*-2-acetylthiomethyl*cyclo*pentylmethyl acetate (3·6 g.) gave *trans*-2-methyl*cyclo*pentylmethanol (0·85 g.), b. p. 110—111°/81 mm., n_D^{18} 1·4531 (Found: C, 73·1; H, 12·45%). The 3 : 5-*dinitrobenzoate* formed small plates [from light petroleum (b. p. 60—80°)], m. p. 56° (Found: C, 54·8; H, 5·4; N, 9·1%); and the α-naphthylurethane, felted needles, m. p. 98° [from light petroleum (b. p. 60—80°)] (Found: C, 76·2; H, 7·6; N, 5·1%).

Nenitzescu and Vantu (*loc. cit.*) give b. p. 171—172°/758 mm., n_D^{20} 1·4512, for their alcohol of unknown configuration. Pines and Hoffman (*loc. cit.*) give b. p. 103°/53 mm., n_D^{20} 1·4533 (α-naphthylurethane, m. p. 98·5—99·5°).

Added in Proof.—Professor Pines has very kindly provided us with a sample of his carbinol;

the α-naphthylurethane prepared from it is identical (m. p. and mixed m. p.) with our *trans*-derivative of m. p. 98°. The trans-*phenylurethane*, which earler had failed to crystallise, subsequently solidified and from a concentrated solution in light petroleum (b. p. 40—60°) formed nodules, m. p. 47—48° (Found: C, 71·9; H, 8·1; N, 6·2%); it follows that the alcohol obtained by Anziani and Cornubert (*loc. cit.*) (phenylurethane, m. p. 92—94°), was not a 2-methyl-*cyclo*pentylmethanol.

This work was carried out during the tenure (by A. G. P.) of a University of London Postgraduate Studentship. Microanalyses were by Mr. F. H. Oliver and his staff (Organic Microanalytical Laboratory).

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The Disproportionation of Di-[2-(N-2′-aminobenzylformamido)propenyl] Disulphide.

By P. Sykes.

[Reprint Order No. 6226.]

A 2-aminobenzyl analogue of thiamine disulphide has been prepared and its disproportionation in heated hydroxylic solvents studied. Its breakdown exactly parallels that of thiamine disulphide, yielding a thiochrome analogue and a thiamine thiazol-2-one (Sykes and Todd, *J.*, 1951, 534) analogue; both of these have been synthesised.

In previous papers (Sykes and Todd, *J.*, 1951, 534; Sykes, *Angew. Chem.*, 1954, **66**, 452), a mechanism was suggested for the disproportionation of thiamine disulphide, in hot, high-boiling hydroxylic solvents, to thiochrome and thiamine thiazol-2-one, and evidence has been adduced in its support. Thiamine disulphide was the only case in which such a disproportionation had been observed and, as much of the evidence turned on the resistance to breakdown exhibited by suitably substituted disulphides (Nesbitt and Sykes, *J.*, 1954, 4581), further confirmation was sought by studying another disulphide, di-[2-(*N*-2′-aminobenzylformamido)propenyl] disulphide (II), in which groups believed to be essential for the ready occurrence of disproportionation were present.

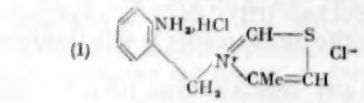
3-2′-Aminobenzyl-4-methylthiazolium chloride hydrochloride (I) was converted into the disulphide (II) by oxidation in alkaline solution with iodine or hydrogen peroxide, though the latter leads to some simultaneous attack on the benzene nucleus. This compound, like several other disulphides derived from thiazolium derivatives, retains a wide variety of solvents of crystallisation most tenaciously.

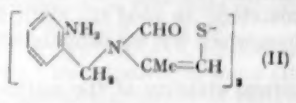
When a solution of the disulphide (II) was refluxed in *iso*butanol, the colour darkened and decomposition took place. It proved impossible to separate the fragments by fractional crystallisation, so the mixture was treated with phenyl *iso*cyanate to render neutral any product still containing an amino-group. Separation with hydrochloric acid then led to the isolation of 3′:4′-dihydro-4-methylquinazolino(2′:3′-2:3)thiazole (III) (the analogue of thiochrome) and 3-2′-phenylureidobenzyl-4-methylthiazol-2-one (IV; R = NH·CO·NHPh, X = O) (the phenyl *iso*cyanate derivative of the analogue of thiamine thiazol-2-one). For comparison both of these compounds were synthesised.

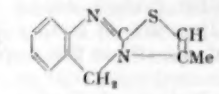
A suitable starting material for the thiazolone (IV) was 2-cyanocarbanilide (V; R = CN) which was to be converted into the amine (V; R = CH_2·NH_2) and thence into the thiazol-2-one (cf. Sykes, *J.*, 1951, 2507). Hydrogenation of a very dilute solution of the cyanide in propan-2-ol (cf. Nesbitt and Sykes, *J.*, 1954, 3057) in the presence of Raney nickel led only to the corresponding secondary amine, and there was no uptake of hydrogen in the presence of platinum or palladium-charcoal catalysts in glacial acetic acid, alone or containing acetic anhydride. Attempted hydrogenation in the presence of anhydrous ammonia yielded the cyclised product (VI; R = Ph, R′ = NH, X = O), there being no reduction. This ring-closure takes place extremely rapidly in the cold in the presence of

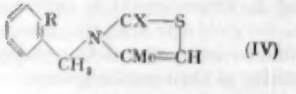
a trace of basic catalyst. Attempted reduction with acid reducing agents yielded only the quinazoline-dione (VI; R = Ph, R′ = X = O), presumably through initial hydrolysis of the cyano-group.

It is not possible to carry out the desired series of reactions with 2-aminobenzylamine owing to the preferential formation of tetrahydroquinazoline derivatives. Reaction of

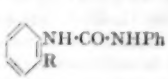








2-nitrobenzylamine, however, with carbon oxysulphide in the presence of one equivalent of alkali, followed by shaking with chloroacetone, led to the separation, apparently, of the thiolcarbamate (VII; R = NO_2, R′ = CH_2Ac, X = O) (a small amount of di-2-nitrobenzylurea is obtained as a by-product in the first stage). Replacement of carbon oxysulphide by carbon disulphide apparently yielded the corresponding dithiocarbamate (VII; R = NO_2, R′ = CH_2Ac, X = S). Both these compounds exhibited no ketonic properties,



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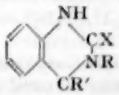
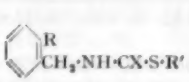


(VI)



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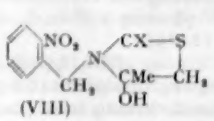

(VIII)

however, and the infrared spectrum of the supposed dithiocarbamate showed no carbonyl absorption; it did, however, exhibit a hydroxyl band. The infrared spectrum of the supposed thiolcarbamate did show a carbonyl band at 6·03 μ but this is more characteristic of a substituted amide than of a simple ketonic group, as is confirmed by the similar absorption at 6·09 μ of the thiolcarbamate of unequivocal structure (VII; R = H, R′ = CH_2·C_6H_4·NO_2-*p*, X = O) prepared for comparison. The slight shift of the band is not unexpected in that the carbon atom adjacent to nitrogen in the structure (VIII; X = O) is electronegative, making the nitrogen atom less basic than in the model (VII) and resulting in electron transfer to the adjacent CO group, thereby increasing the contribution made by the $>C^+-O^-$ structure, which would be expected to lead to a slight shift in the observed direction. Thus the two supposed thiocarbamates have, not the expected structure (VII; R = NO_2, R′ = CH_2Ac, X = O or S), but the cyclic formula (VIII; X = O or S) (cf. Yoshida, *Pharm. Bull.*, **1954**, **2**, 249). Attempts to form a derivative from the tertiary hydroxyl group of the thiazolid-2-thione with phenyl *iso*cyanate were unsuccessful, while attempted benzoylation caused dehydration, yielding the thiazol-2-thione (IV; R = NO_2, X = S). It is probable that this dehydration proceeds *via* an unstable *O*-benzoyl derivative, as the starting material is stable in the presence of alkali or pyridine alone; dehydration is promoted only by acid catalysis or by heating the compound above its m. p. This behaviour is in marked contrast to that of the simpler dithiocarbamate (VII) which yielded a stable benzoyl derivative. The compounds (VIII) are also unaffected by hydrogen peroxide in alkaline solution while the model compounds (VII) yielded di-4-nitrobenzyl disulphide.

Aqueous-ethanolic hydrogen chloride converted the compounds (VIII) very readily into the thiazol-2-ones (IV; R = NO_2, X = O and S, respectively). Reduction with titanous chloride yielded the corresponding amino-derivatives (IV; R = NH_2, X = O and S, respectively); the infrared spectrum of the aminothiazol-2-one disclosed considerable hydrogen bonding between the amino- and the carbonyl group. Reaction of the aminothiazol-2-one with phenyl *iso*cyanate then yielded the desired thiazolone moiety (IV; R = NH·CO·NHPh, X = O).

The thiochrome analogue (III) might be expected to be obtained by potassium ferricyanide oxidation of an alkaline solution of the salt (I), analogous to the formation of thiochrome from thiamine. The initial attack of a one-electron oxidising agent is on the activated benzene nucleus, however, and only dark polymers were obtained, just as with, *e.g.*, aniline. The desired compound was, however, formed on condensation of 1 : 2 : 3 : 4-tetrahydro-2-thioquinazoline (VI; R = H, R′ = H_2, X = S) (Busch, *J. prakt. Chem.*, **1895**, **51**, 128) with chloroacetone, to yield the hydrochloride of the base (III); this with alkali yielded a pseudo-base which was not dehydrated to the anhydro-base so readily as with thiochrome itself.

The thermal stability of the amino-thiazolone and -thiazol-2-thione (IV; R = NO_2, X = O and S, respectively) is considerable and neither cyclises, except under extreme conditions, to yield the tricyclic compound (III). They are, in fact, quite as stable as thiamine thiazol-2-one and -2-thione (Sykes and Todd, *loc. cit.*) in this respect despite the greater basicity of their amino-groups.

Experimental

Di-[2-(N-2′-aminobenzylformamido)propenyl] Disulphide (II).—3-2′-Aminobenzyl-4-methylthiazolium chloride hydrochloride (I) (Livermore and Sealock, *J. Biol. Chem.*, **1947**, **167**, 699) (0·82 g.) in water (5 ml.) was treated with 1·065N-sodium hydroxide (8·35 ml., 3 equiv.), and hydrogen peroxide (20-vol.; 0·84 ml., 0·5 equiv.) was then added dropwise to the yellow solution. The separated, sticky solid was set aside for 1 hr., then collected and washed with water. The *disulphide* crystallised from ethanol–acetone as pale yellow needles (0·22 g., 35%), m. p. 136° (decomp.) (Found: C, 59·7; H, 6·0; N, 12·6. $C_{22}H_{26}O_2N_4S_2$ requires C, 59·7; H, 5·9; N, 12·7%).

Heating of Di-[2-(N-2′-aminobenzylformamido)propenyl] Disulphide (II) *in* iso*Butanol.*—The foregoing disulphide (2·2 g.) in dry *iso*butanol (75 ml.) was refluxed under nitrogen for 4 hr.; some darkening took place. The solvent was removed at room temperature/10^{-4} mm., the residue taken up in dry toluene and again evaporated under reduced pressure to remove the last traces of *iso*butanol. The residue was taken up in dry benzene and heated with phenyl *iso*cyanate (0·6 g.) at 50° for 1 hr. Evaporation at room temperature/10^{-4} mm. yielded an orange gum. This was dissolved in ether (150 ml.), and the ethereal solution extracted several times with 3N-hydrochloric acid. The ethereal extract was washed with water, dried (Na_2CO_3), and evaporated under reduced pressure, yielding a yellow oil. Crystallisation from ethanol (charcoal) yielded 3-2′-phenylureidobenzyl-4-methylthiazol-2-one (IV; R = NH·CO·NHPh, X = O) as colourless needles, m. p. and mixed m. p. 165° (Found: C, 63·7, H, 4·8; N, 12·6. Calc. for $C_{18}H_{17}O_2N_3S$: C, 63·6; H, 5·0; N, 12·4%).

The hydrochloric acid extract was washed with ether and made alkaline with 3N-sodium hydroxide, and the separated oil then extracted with ether. The ethereal extract was dried (Na_2CO_3) and a slow stream of dry hydrogen chloride passed through it, a crystalline hydrochloride separating. Recrystallisation from *n*-butanol yielded 3′ : 4′-dihydro-4-methylquinazolino(2′ : 3′-2 : 3)thiazole hydrochloride as colourless plates, m. p. and mixed m. p. 282° (decomp.) (Found: C, 55·0; H, 4·8; N, 11·4. Calc. for $C_{11}H_{10}N_2S$,HCl: C, 55·1; H, 4·6; N, 11·7%).

Reduction of 2-Cyanocarbanilide (V; R = CN).—(*a*) A solution of 2-cyanocarbanilide (1 g.) in *iso*propanol (200 ml.) was hydrogenated at room temperature and atmospheric pressure with freshly prepared W-7 Raney nickel (3 g.), the theoretical volume of hydrogen being absorbed in 45 min. The mixture was then filtered through "Hyflo Supercel" and evaporated to dryness under reduced pressure yielding a pink gum. Trituration with ether and N-hydrochloric acid induced crystallisation. Recrystallisation from ethanol yielded *di-(2-phenylureidobenzyl)amine hydrochloride* as needles, m. p. 177° (Found: C, 67·2; H, 5·7; N, 14·1. $C_{28}H_{27}O_2N_5$,HCl requires C, 67·8; H, 5·6; N, 14·0%). Hydrogenation did not occur in the presence of acetic or hydrochloric acids with platinum or palladium catalysts.

(*b*) The above reduction was repeated with propan-2-ol saturated with dry ammonia at 0° as solvent, at room temperature/75 atm. for 11 hr. Removal of the catalyst and evaporation of the solution yielded 1 : 2 : 3 : 4-*tetrahydro-4-imino-2-oxo-3-phenylquinazoline* (VI; R = Ph, R′ = NH, X = O) which crystallised from aqueous alcohol as prisms, m. p. 224° (Found: C, 70·7; H, 4·9; N, 17·9. $C_{14}H_{11}ON_3$ requires C, 70·9; H, 4·6; N, 17·7%), insoluble in water, soluble in dilute hydrochloric acid [hydrochloride, m. p. 250° (decomp.)] from which it is precipitated unchanged by aqueous ammonia or potassium carbonate but not by sodium hydroxide.

The isomerisation of 2-cyanocarbanilide may also be effected very rapidly with aqueous ammonia or sodium hydroxide.

(*c*) A solution of 2-cyanocarbanilide (1 g.) in ethanol (100 ml.) was diluted with 3N-hydrochloric acid (30 ml.), and granulated zinc (2·5 g.) added. The mixture was warmed slightly and then kept at room temperature for 24 hr. Evaporation under reduced pressure led to the separation of colourless crystals of 1 : 2 : 3 : 4-tetrahydro-2 : 4-dioxo-3-phenylquinazoline (VI; R = Ph, R′ = X = O) (Paal, *Ber.*, 1894, **27**, 978), needles, m. p. 272° (from ethanol) (Found: C, 70·3; H, 4·0; N, 11·6. Calc. for $C_{14}H_{10}O_2N_2$: C, 70·5; H, 4·2; N, 11·8%).

4-Hydroxy-4-methyl-3-2′-nitrobenzylthiazolid-2-one (VIII; X = O).—2-Nitrobenzylamine hydrochloride (Ing and Manske, *J.*, 1926, 2350) (4·7 g.) was dissolved in water (150 ml.) and treated with N-sodium hydroxide (50 ml., 2 equiv.), and a rapid stream of pure carbon oxysulphide then passed through the solution for 45 min. The pale yellow solution (pH now 7·5) was filtered to remove a trace of di-2-nitrobenzylurea, chloroacetone (2·6 g., 1·1 equiv.) added, and the mixture shaken for 10 min. The crystals which separated were filtered off and washed with water. Recrystallisation from ethanol yielded the *thiazolid-2-one* (4·2 g., 63%) as colourless needles, m. p. 140° (decomp.) (Found: C, 49·3; H, 4·4; N, 10·6. $C_{11}H_{12}O_4N_2S$ requires C, 49·3; H, 4·5; N, 10·5%).

Similar reaction of the amine with carbon disulphide and alkali, followed by chloroacetone, yielded *4-hydroxy-4-methyl-3-2′-nitrobenzylthiazolid-2-thione* (VIII; X = S), which crystallised from ethanol (charcoal) as prisms (84%), m. p. 159° (decomp.) (Found: C, 46·8; H, 4·1; N, 10·0. $C_{11}H_{12}O_3N_2S_2$ requires C, 46·5; H, 4·2; N, 9·9%).

In attempted reactions with phenyl *iso*cyanate in benzene and with an alkaline solution of hydrogen peroxide in aqueous acetone unchanged starting material was recovered. Attempted benzoylation of the thione (VIII; X = S) under Schotten–Baumann conditions or in pyridine caused dehydration to the thiazol-2-thione (IV; X = S).

S-4-Nitrobenzyl N-Benzylthiolcarbamate (VII; R = H, R′ = 4-CH_2·C_6H_4·NO_2, X = O).—Benzylamine (10·7 g.) in ethanol (200 ml.) was treated with a stream of carbon oxysulphide until no more solid separated. Ethanol (100 ml.) was then added and the mixture warmed till all the solid had dissolved. 4-Nitrobenzyl bromide (10 g., 1 equiv.) was added and the solution set aside to crystallise; a further crop was obtained by warming the mother-liquors and diluting them slightly with water. The crystals were collected and washed with ethanol. Recrystallisation from ethanol yielded the *thiolcarbamate* (10 g., 67%) as leaflets, m. p. 137° (Found: C, 59·8; H, 4·8; N, 9·2. $C_{15}H_{14}O_3N_2S$ requires C, 59·6; H, 4·6; N, 9·3%).

Similar reaction of the amine with carbon disulphide and 4-nitrobenzyl bromide yielded *4-nitrobenzyl N-benzyldithiocarbamate* (VII; R = H, R′ = 4-CH_2·C_6H_4·NO_2, X = S), needles (70%) (from aqueous ethanol), m. p. 91° (Found: C, 56·8; H, 4·5; N, 8·8. $C_{15}H_{14}O_2N_2S_2$ requires C, 56·6; H, 4·4; N, 8·8%).

The dithiocarbamate (1 g.) in ethanolic acetone was treated with an excess of hydrogen peroxide (20-vol.) and an excess of N-sodium hydroxide. The solution immediately became dark red but subsequently lightened a little. After 5 min., water was added and the flocculent precipitate was collected and washed with water. Recrystallisation from ethanol yielded needles of di-4-nitrobenzyl disulphide (Price and Twiss, *J.*, 1909, **95**, 1728), m. p. and mixed m. p. 126° (Found: C, 50·3; H, 3·9; N, 8·0. Calc. for $C_{14}H_{12}O_4N_2S_2$: C, 50·0; H, 3·6; N, 8·3%).

The dithiocarbamate (1 g.) in dry pyridine (5 ml.) was treated with benzoyl chloride (0·45 g., 1 equiv.). After 4 hr. at room temperature the solution was poured into warm water with stirring. The aqueous phase was decanted and the sticky gum stirred with a further portion of water; it then began to crystallise on scratching. The crystals were collected and washed with water. Recrystallisation from ethanol–acetone (charcoal) yielded yellow needles of the *benzoyl derivative*, m. p. 114° (Found: C, 63·0; H, 4·3; N, 6·6. $C_{22}H_{16}O_3N_2S_2$ requires C, 62·6; H, 4·3; N, 6·6%).

4-Methyl-3-2′-nitrobenzylthiazol-2-one (IV; R = NO_2, X = O).—The foregoing thiazolid-2-one (0·75 g.) was dissolved in ethanol (50 ml.), 3N-hydrochloric acid (10 ml.) was added (cf. Sykes, *J.*, 1951, 2507), and the solution brought just to the b. p. After 5 min. it was again heated to the b. p., diluted with water, and allowed to cool. The crystals which separated were filtered off and washed with ethanol. Recrystallisation from ethanol yielded the *thiazol-2-one* (0·49 g., 70%) as colourless needles, m. p. 163° (Found: C, 53·0; H, 4·2; N, 11·1. $C_{11}H_{10}O_3N_2S$ requires C, 52·8; H, 4·0; N, 11·2%).

Similar treatment of the above thiazolid-2-thione yielded *4-methyl-3-2′-nitrobenzylthiazol-2-thione* (IV; R = NO_2, X = S), which crystallised from ethanol (charcoal) as colourless needles (56%), m. p. 129° (Found: C, 49·8; H, 4·0; N, 10·5. $C_{11}H_{10}O_2N_2S_2$ requires C, 49·6; H,

3·8; N, 10·5%). Ring closure was also effected (71%) by heating the dithiocarbamate above its m. p. till gas evolution had ceased (cf. Sykes and Todd, *J.*, 1951, 534).

3-2′-Aminobenzyl-4-methylthiazol-2-one (IV; R = NH_2, X = O).—The foregoing thiazol-2-one (1 g.) in ethanol (65 ml.) was heated to 70° and acid titanous chloride solution [15%; 25 ml., to which 3N-hydrochloric acid (20 ml.) has been added] was added dropwise. The solution was evaporated under reduced pressure to remove ethanol and treated with solid sodium carbonate till faintly cloudy and an excess of saturated aqueous picric acid then run into the stirred solution. The separated picrate was collected after 48 hr., washed with water, then shaken repeatedly with portions of ether and aqueous sodium hydroxide (10%). The combined ethereal extracts were filtered, washed with water, and extracted twice with 3N-hydrochloric acid and finally with water. The combined aqueous extract was treated with solid sodium carbonate until no more solid separated. Recrystallisation from ethanol yielded the *aminothiazol-2-one* as colourless needles (0·4 g., 45%), m. p. 104° (Found: C, 59·7; H, 5·3; N, 13·0. $C_{11}H_{12}ON_2S$ requires C, 60·0; H, 5·5; N, 12·7%).

Similar reduction of the above thiazol-2-thione (the decomposition of the picrate was less satisfactory, however) yielded *3-2′-aminobenzyl-4-methylthiazol-2-thione* (IV; R = NH_2, X = S), prisms (29%) (from ethanol), m. p. 136° (Found: C, 56·2; H, 5·0; N, 12·1. $C_{11}H_{12}N_2S_2$ requires C, 56·0; H, 5·1; N, 11·9%).

4-Methyl-3-2′-phenylureidobenzylthiazol-2-one (IV; R = NH·CO·NHPh, X = O).—The foregoing aminothiazol-2-one (0·3 g.) in dry benzene (10 ml.) was treated with phenyl *iso*cyanate (0·17 g., 1 equiv.) in benzene (1·5 ml.) and the solution refluxed for 5 hr. Removal of the benzene yielded a gum which crystallised on trituration with ethanol. Recrystallisation from ethanol yielded the *phenylureidothiazol-2-one* as needles (0·35 g., 74%), m. p. 165° (Found: C, 63·8; H, 4·9; N, 12·5. $C_{18}H_{17}O_2N_3S$ requires C, 63·6; H, 5·0; N, 12·4%).

3′:4′-Dihydro-4-methylquinazolino(2′:3′-2:3)thiazole (III).—A solution of 1:2:3:4-tetrahydro-2-thioquinazoline (VI; R = H, R′ = H_2, X = S) (Busch, *J. prakt. Chem.*, 1895, **51**, 128) (1 g.) in dry acetone (50 ml.) was refluxed with redistilled chloroacetone (3 g.) for 4 hr. The separated crystals were then collected and washed with acetone. Recrystallisation from *n*-butanol yielded the *quinazolinothiazole hydrochloride* as colourless plates (0·7 g., 48%), m. p. 282° (decomp.) (Found: C, 54·9; H, 4·8; N, 11·5. $C_{11}H_{10}N_2S,HCl$ requires C, 55·1; H, 4·6; N, 11·7%).

Treating a solution of the hydrochloride in aqueous ethanol with ammonia, collecting of the product, and recrystallising it from *n*-butanol yielded the *base* as colourless needles, m. p. 174° (decomp.) (Found: C, 60·2; H, 5·4; N, 12·6. $C_{11}H_{10}N_2S,H_2O$ requires C, 60·0; H 5·5; N, 12·7%).

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Perimidine Dyes and Intermediates.

By R. A. JEFFREYS.

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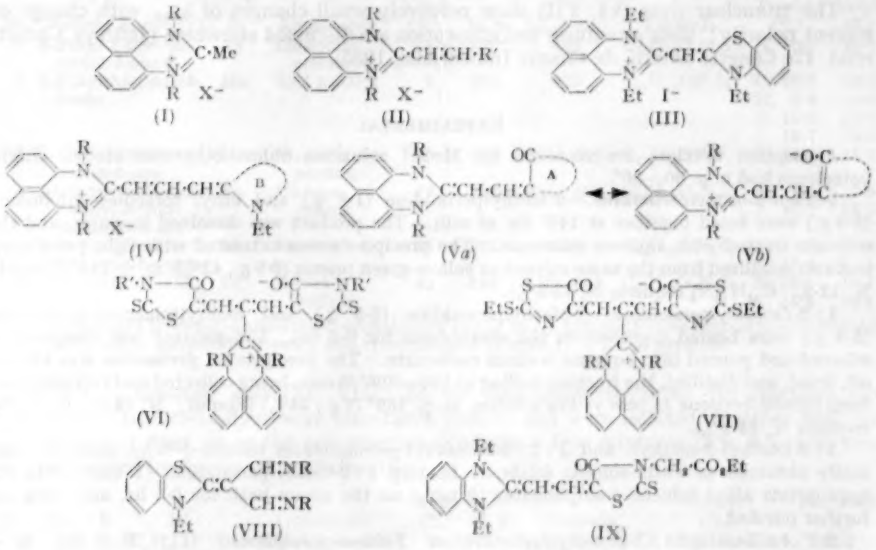
Intermediates, cyanine and *mero*cyanine dyes, all possessing a perimidine ring, have been prepared. The dihydroperimidine ring system has strong electron-releasing powers, indicated by the reversal of Kundt's rule in some *mero*cyanines. An abnormal condensation between 2-methylperimidinium salts and ethoxymethylene-keto-heterocyclic intermediates provides trinuclear *mero*cyanines, which may be considered as chain-substituted mesoionic oxonols.

ONE of the strongest electron-releasing (−*M*) heterocyclic systems used in the preparation of cyanine and *mero*cyanine dyes is benziminazoline (cf. Brooker, Keyes, Sprague, Van Dyke, Van Lare, Van Zandt, White, Cressman, and Dent, *J. Amer. Chem. Soc.*, 1951, **73**, 5332). Perimidine is related to benziminazole through its structural isomers the naphthiminazoles, and a comparison of the properties of related dyes was therefore of interest.

Low yields of pure 1-alkyl-2-methylperimidine intermediates were obtained, with some

difficulty, by fusing 2-methylperimidine with alkyl toluene-*p*-sulphonates, followed by basification of the resulting salts. They were readily quaternized by fusion with alkyl esters on the steam-bath, forming 1 : 3-dialkyl-2-methylperimidinium salts (I). The intermediate (I) condensed with *O*-ethyl*iso*formanilide (at elevated temperatures) to form 2-2′-anilinovinyl intermediates (II; R′ = NHPh); with *p*-dimethylaminobenzaldehyde (in pyridine with a drop of piperidine) to form a 2-*p*-dimethylaminostyryl dye (II; R′ = $C_6H_4{\cdot}NMe_2$); with a 3-ethyl-2-ethylthiobenzothiazolium salt to form a lemon-yellow



monomethincyanine (III); and with 2-2′-acetanilidovinyl heterocyclic salts (in ethanol in the presence of triethylamine) to form various trimethincyanines (IV; see Table 2). The 2-2′-anilinovinyl intermediates (II; R′ = NHPh) reacted with ketomethylene heterocyclic compounds to give dimethin*mero*cyanines (V).

In an alternative method of preparing the last dyes, 2-methylperimidinium salts (I) were condensed with ethoxymethylene-keto-heterocyclic compounds in alcoholic triethylamine according to a known general synthesis (Kendall and Fry, B.P. 544,647; Cook, Harris, and Shaw, *J.*, 1949, 1435; Aubert, Knott, and Williams, *J.*, 1951, 2185). In each reaction two dyes were formed and, in three reactions, pairs of dyes were isolated. The lighter dye of each pair was a *mero*cyanine (V), and the deeper one proved to be a trinuclear dye (VI, VII). Dyes of type (VI) possessing nuclei other than perimidine have been described by Hamer, Rathbone, and Winton (*J.*, 1949, 1113), who used dianilo-intermediates (VIII) in their syntheses.

TABLE 1. *Absorption maxima* (mμ) *of dyes in various solvents* (*i* indicates an inflection).

	Benzene	MeOH	Aq. MeOH (1 : 2)
Va; R = Me, A = 3-allyl-2-thiothiazolid-4-one	476*i*, 498	482*i*, 502	482*i*, 503
Va; R = Et, A = 3-ethoxycarbonylmethyl-2-thiothiazolid-4-one	477*i*, 503	484*i*, 505	483*i*, 505
Va; R = Me, A = 2-ethylthiothiazol-5-one	495	476	466
Va; R = Me, A = 3-methyl-2-thiothiazolid-5-one	497*i*, 523	508	495
IX	488*i*, 513	488*i*, 508	500
VI; R = Me, R′ = allyl	525*i*, 547	520*i*, 542	517*i*, 541
VI; R = Et, R′ = $EtO_2C{\cdot}CH_2$	522*i*, 545	512*i*, 536	512*i*, 536
VII; R = Me	529*i*, 570	535*i*, 566	541*i*, 572
VII; R = Et	—	530*i*, 569	—

The strong electron-releasing power of the dihydroperimidine nucleus is indicated by a reversal of Kundt's rule for some derived *mero*cyanine dyes (cf. Brooker *et al.*, *loc. cit.*). Thus, in solvents of increasing polarity and dipole moment (see Table 1), hypsochromic shifts of 10—19 mμ occur for perimidine dyes possessing strongly $+M$ thiazol-5-one and thiazolid-5-one rings, whereas the corresponding thiazolid-4-one dyes (weaker $+M$ effect) show small bathochromic shifts. The benziminazole dye with a thiazolid-4-one ring (IX), however, exhibits hypsochromic shifts of 5 and 8 mμ, indicating the still stronger $-M$ effect of the benziminazoline nucleus compared with that of dihydroperimidine.

The trinuclear dyes (VI, VII) show relatively small changes of $\lambda_{max.}$ with change of solvent polarity; their structures and absorption are discussed elsewhere (Jeffreys, Compt. rend. 17e Congrès Intern. de Chimie Industrielle, 1955).

Experimental

Absorption maxima are recorded for MeOH solutions unless otherwise stated. Light petroleum had b. p. 60—80°.

1-*Ethyl*-2-*methylperimidine*.—2-Methylperimidine (1·8 g.) and ethyl toluene-*p*-sulphonate (2·0 g.) were fused together at 140° for 45 min. The product was dissolved in water, and the solution treated with aqueous ammonia. The precipitate was extracted with light petroleum, and recrystallized from the same solvent as yellow-green prisms (0·9 g., 43%), m. p. 115° (Found: N, 13·2. $C_{14}H_{14}N_2$ requires N, 13·3%).

1 : 2-*Dimethylperimidine*.—2-Methylperimidine (5·5 g.) and methyltoluene-*p*-sulphonate (5·6 g.) were heated together on the steam-bath for 0·5 hr. The product was dissolved in ethanol and poured into aqueous sodium carbonate. The precipitated *perimidine* was filtered off, dried, and distilled, the fraction boiling at 196—200°/6 mm. being collected and recrystallized from ligroin–benzene as pale yellow needles, m. p. 159° (2 g., 34%) (Found: N, 14·2. $C_{13}H_{12}N_2$ requires N, 14·3%).

1 : 3-Diethyl-2-methyl- and 1 : 2 : 3-trimethyl-perimidinium toluene-*p*-sulphonate (I) were easily obtained as water-soluble solids by heating 1 : 2-dialkylperimidines (1 mol.) with the appropriate alkyl toluene-*p*-sulphonates (1 mol.) on the steam-bath for 0·5 hr. and were not further purified.

2-2′-*Anilinovinyl*-1 : 3-*dimethylperimidinium Toluene*-p-*sulphonate* (II; R = Me, R′ = NHPh, X = toluene-*p*-sulphonate).—1 : 2 : 3-Trimethylperimidinium toluene-*p*-sulphonate (5·1 g.) and *O*-ethyl*iso*formanilide (2·1 g.) were heated together at 140° for 1 hr. Ethanol was added to the gum, and the solid which formed recrystallized from ethanol–ether as a yellow powder (4·5 g., 77%), m. p. 216° (decomp.) (Found: N, 8·7; S, 6·7. $C_{28}H_{27}O_3N_3S$ requires N, 8·7; S, 6·6%).

2-2′-*Anilinovinyl*-1 : 3-*diethylperimidinium Iodide* (II; R = Et, R′ = NHPh, X = I).—1 : 3-Diethyl-2-methylperimidinium toluene-*p*-sulphonate (4·1 g.) and *O*-ethyl*iso*formanilide (1·5 g.) were heated together at 140° for 2 hr. and the resulting gum dissolved in ethanol. This solution was poured into aqueous potassium iodide. The *product* was filtered off and recrystallized from ethanol–ether as dark brown prisms (3 g., 64%), m. p. 233° (decomp.) (Found: N, 9·1; I, 27·4. $C_{23}H_{24}N_2I$ requires N, 9·0; I, 27·1%).

Table 2. [1 *or* 3-*Ethyl*-2-*B*][1 : 3-*dialkyl*-2-*perimidine*]*trimethincyanine dyes* (IV).
(*i* indicates an inflection.)

Heterocycle B	R	X	Appearance	M. p.	$\lambda_{max.}$ (mμ)	Formula	Found (%)	Reqd. (%)
Benzoxazoline	Et	ClO_4	Orange-brown [a]	212°	458*i*, 482	$C_{27}H_{24}O_6N_3Cl$	N, 8·2	8·2
Benzothiazoline	Me	I	Bronze [b]	233	499	$C_{25}H_{24}N_3SI$	N, 7·9	8·0
							S, 6·1	6·1
							I, 24·3	24·2
1 : 2-Dihydroquinoline	Me	I	Indigo [c]	252	510*i*, 539	$C_{27}H_{26}N_3I$	N, 8·0	8·1
							I, 24·3	24·4

[a] Needles from methanol–ether. [b] Needles from pyridine–ether. [c] From methanol, after chromatography on alumina.

2-p-*Dimethylaminostyryl*-1 : 3-*dimethylperimidinium Iodide* (II; R = Me, R′ = *p*-$Me_2N{\cdot}C_6H_4$, X = I).—1 : 2 : 3-Trimethylperimidinium toluene-*p*-sulphonate (2·6 g.) and *p*-dimethylaminobenzaldehyde (1 g.) in pyridine (40 c.c.) with piperidine (2 drops) were refluxed for 2 hr. and the

solution poured into aqueous potassium iodide. The precipitated *dye* recrystallized from pyridine–methanol as orange needles (0·1 g.), m. p. 257° (decomp.), $\lambda_{max.}$ 439 mμ (Found: N, 9·0; I, 27·1. $C_{23}H_{24}N_3I$ requires N, 8·9; I, 27·1%).

[*3-Ethyl-2-benzothiazole*][*1 : 3-diethyl-2-perimidine*]*methincyanine Iodide* (III).—1 : 3-Diethyl-2-methylperimidinium toluene-*p*-sulphonate (1·2 g.) and 3-ethyl-2-ethylthiobenzothiazolium toluene-*p*-sulphonate (1·2 g.) with triethylamine (0·4 c.c.) in ethanol (8 c.c.) were refluxed for

TABLE 3. *Dimethin*merocyanine *dyes* (V, IX). (*i* indicates an inflection.)

No.	Nucleus A, dye (V)	R	Appearance	Yield (%)	M. p.	$\lambda_{max.}$ (mμ)	Formula	Found (%)	Reqd. (%)
1	3-Ethyl-2-thio-oxazolid-4-one [a]	Et	Chocolate prisms	48	203°	480	$C_{23}H_{22}O_2N_2S$	N, 10·7	10·7
2	2-Ethylthiothiazol-5-one	Me	Red needles	7	212	476	$C_{20}H_{18}ON_2S_3$	C, 63·1 H, 5·3 N, 10·9 S, 16·7	63·0 5·0 11·0 16·8
3	3-Allyl-2-thiothiazolid-4-one	Me	Magenta needles	10	217	482*i*, 502	$C_{21}H_{18}ON_2S_3$	S, 16·3	16·3
4	3-Ethoxycarbonylmethyl-2-thiothiazolid-4-one	Et	Maroon prisms	14	208	484*i*, 505	$C_{24}H_{22}O_3N_2S_3$	N, 9·1 S, 13·7	9·0 13·7
5	3-Methyl-2-thiothiazolid-5-one [a]	Me	Maroon [b]	35	282	508	$C_{19}H_{17}ON_2S_3$	N, 11·4 S, 17·4	11·4 17·4
6	Dye (IX)	Et	Brown leaflets	30	184	488*i*, 508	$C_{30}H_{32}O_2N_2S_3$	N, 10·0 S, 15·4	10·1 15·4

[a] Prepared from 2-2′-anilinovinylperimidinium salt (1 mol.), ketomethylene heterocyclic compound (1 mol.), acetic anhydride (1 mol.), and triethylamine (2 mols.). [b] From pyridine.

TABLE 4. *Trinuclear dyes* (VI, VII). In the dimethin*mero*cyanine dye reactions (see above) trinuclear dyes were sometimes formed and were isolated, together with the dinuclear dyes, or as the sole reaction products. Dye mixtures (2/9, 3/7, 4/8) were separated by fractional crystallization.

No.	Dye	R	R′	Appearance	Yield (%)	M. p.	Formula	Found (%)	Required (%)
7	VI	Me	C_2H_5	Red-brown needles [a]	7	216°	$C_{34}H_{34}O_2N_4S_4$	S, 22·2	22·2
8	VI	Et	$CH_2{\cdot}CO_2Et$	Maroon leaflets [b]	19	184	$C_{32}H_{32}O_6N_4S_4$	C, 55·4; H, 4·8; N, 8·1; S, 18·4	55·2; 4·6; 8·1; 18·4
9	VII	Me	—	Bronze plates [b]	25	299	$C_{36}H_{34}O_2N_4S_4$	C, 56·4; H, 4·3; N, 10·0; S, 23·3	56·5; 4·3; 10·1; 23·2
10	VII	Et	—	Gold needles [c]	20	261	$C_{34}H_{34}O_2N_4S_4$	S, 22·0	22·1

[a] From pyridine–methanol–ether. [b] From pyridine–ethanol. [c] From ethanol.

30 min., and the solution was poured into aqueous potassium iodide. The *dye* was filtered off and recrystallized from ethanol as a fluffy yellow powder (0·1 g.), m. p. 207°, $\lambda_{max.}$ 385 mμ (Found: N, 8·0. $C_{25}H_{25}N_3SI$ requires N, 8·0%).

Trimethincyanines (Table 2).—Three trimethincyanines were prepared by condensing together the 2-methylperimidinium and 2-2′-acetanilidovinyl heterocyclic quaternary salts in ethanol, with triethylamine to remove the acid liberated.

*Dimethin*merocyanines (see Tables 3 and 4).—Unless otherwise stated, these were prepared in ethanol, from 2-methyl-heterocyclic quaternary salts (1 mol.) and ethoxymethylene derivatives of ketomethylene heterocyclic compounds (2 mols.) in the presence of triethylamine (2 mols.).

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The Synthesis of Potential Androgens. Part I.

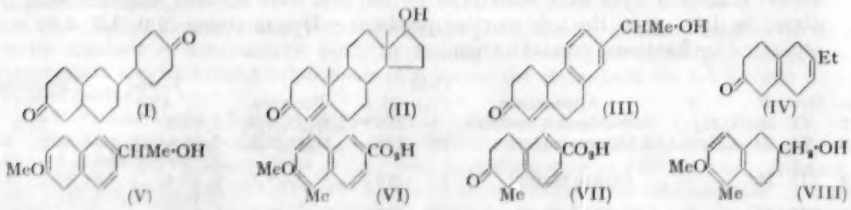
By K. W. Bentley.

[Reprint Order No. 6054.]

Several unsaturated ketones have been prepared by reduction of methoxy-substituted aromatic compounds with sodium and liquid ammonia, in attempts to obtain for androgenic testing substances bearing a superficial resemblance in structure to testosterone.

After the preparation by Wilds and Shunk (*J. Amer. Chem. Soc.*, 1949, **71**, 3266) of a compound (I) containing part of the testosterone (II) skeleton and reported to be feebly androgenic, it was resolved to synthesise other substances in the hope of finding androgenic activity combined with similar partial hormone constitution.

The αβ-unsaturated cyclic ketone structure present in testosterone should be accessible in simpler compounds either by the Mannich base ring-extension method or by reduction of a methoxy-substituted aromatic nucleus with sodium and liquid ammonia, followed by hydrolysis and subsequent isomerisation of the βγ-unsaturated ketone produced. In an attempt to synthesis the ketone (III) by a combination of these methods, 2-acetyl-6-methoxynaphthalene was reduced to the secondary alcohol by Pondorff's method. When this was treated with an excess of sodium in liquid ammonia and alcohol, complete reduction occurred, the product after hydrolysis being 6-ethyl-1 : 2 : 3 : 4 : 5 : 8-hexahydro-2-oxonaphthalene (IV); use of the calculated amount of sodium however gave the dihydro-compound (V) in good yield. The latter with mineral acid could not be hydrolysed without partial dehydration, and this series of reactions was not pursued further.

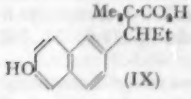


The acid (VI) was available from other work and it was thought possible, though unlikely, that sodium–ammonia reduction of this would lead to the ketone (VII) in which the carboxyl group occupies a position suitable for the addition of the sterol ring D. The free acid could not be reduced, but the ethyl ester was readily reduced, as expected, in the ring carrying the ester substituent, and at the same time at the ester group itself, the product being the alcohol (VIII). This subsidiary result was however not studied further.

It was thought that, despite the inactivity of the substance prepared by Birch and Mukherji (*J.*, 1949, 2531) by the reduction of hexœstrol, reduction of the potent œstrogen (IX) (Horeau and Jaques, *Bull. Soc. chim. France*, 1948, 708) might afford an androgen. In view of the ready elimination of the hydroxyl group under the conditions of the reduction leading to the ketone (IV) the more readily accessible ester (X) was reduced with an excess of sodium, liquid ammonia, and ethanol; as expected, after hydrolysis of the initial product, the ketone (XI) was obtained, nuclear reduction, Bouveault–Blanc reduction, and reductive elimination of the hydroxyl group occurring during the reaction. The ester (X) with an excess of methylmagnesium iodide gave what is believed to be the diol (XII), which could not be isolated and purified without dehydration: reduction, hydrolysis, and distillation of the unpurified material caused extensive dehydration.

Attempted angular methylation of the ester (XIII) by Birch and Robinson's method (*J.*, 1944, 501) afforded only intractable tars. Condensation with methylmagnesium iodide gave a mixture of the diol (XIV; R = Me) and a substance having the composition of a monodehydrated derivative of this, whilst reduction of the ester with lithium aluminium

hydride yielded the alcohol (XIV; R = H). Reduction of the diol (XIV; R = Me) with sodium and liquid ammonia gave the enol ether (XV) by the hydrolysis of which the keto-alcohol (XVI; R = Me) was prepared; a second, further reduced compound was also obtained, and this on hydrolysis yielded the hydroxy-ketone (XVII). Reduction of the simpler diol (XIV; R = H) with sodium and ammonia similarly gave, after hydrolysis, the ketone (XVI; R = H).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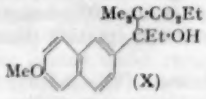
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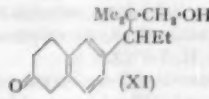
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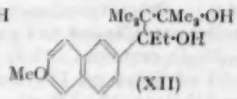
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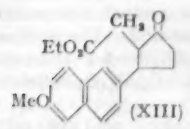
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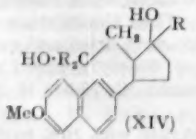
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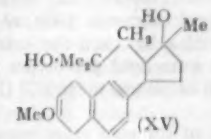
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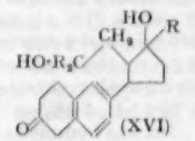
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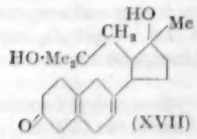
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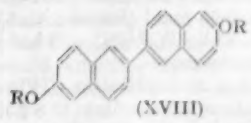
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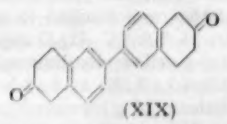
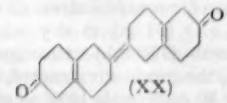

(XIX)

Derivatives of 6 : 6′-dihydroxy-2 : 2′-dinaphthyl (XVIII; R = H) were prepared with the intention of reducing these to the corresponding diketone (XX). The dihydroxydinaphthyl (XVIII; R = H), its dimethyl ether (XVIII; R = Me) and its di-2-hydroxyethyl ether (XVIII; R = CH_2·CH_2·OH) were all prepared by the reduction of 6-bromo-2-naphthol and its ethers by Busch's method (*Ber.*, 1929, **62**, 2612) modified so as to be conveniently carried out under normal pressure. The yields of bimolecular compounds were about 10%. The dimethyl ether (XVIII; R = Me) was too sparingly soluble in all solvents, and the diglyceryl ether [XVIII; R = CH_2·CH(OH)·CH_2·OH] was finally reduced in poor yield with an excess of sodium and liquid ammonia, with triethylene glycol (the only alcohol in which the ether was noticeably soluble even at high temperatures) as the reducing alcohol. The initial reduction product was evidently more soluble in this medium than the starting material, and apparently underwent considerable further reduction, as the product after hydrolysis gave analytical data in accord with the structure (XX) This product was a glass and isomerisation to the αβ-unsaturated ketone, involving the production of a mixture of isomers, may well have accompanied hydrolysis. The reduction of 6-bromo-2-methoxynaphthalene and of 6-acetyl-1-chloro-2-methoxynaphthalene with sodium and ammonia resulted in the loss of the halogen, so that reduction in this way before the bimolecular coupling is not practicable.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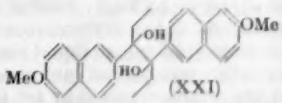
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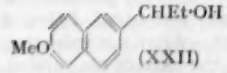
(XXII)

An attempt was made to prepare the naphthalene analogue of hexœstrol, and in this connection 6-methoxy-2-propionylnaphthalene was reduced in 10% yield to the pinacol (XXI), dehydration of which yielded only intractable material. In an attempt to prepare the naphthalene analogue of anethole in order to repeat with this substance Kharasch and Kleimann's hexœstrol synthesis (*J. Amer. Chem. Soc.*, 1943, **65**, 491) the alcohol (XXII) was heated with acetic anhydride: the acetyl ester was obtained, but with formic acid or anhydrous cupric sulphate, only polymers resulted.

Owing to the unsatisfactory nature of all these results [the substances (XI), (XVI; R = Me), (XVI; R = H), and (XX) proved to be androgenically inactive] these reactions were abandoned and investigation turned to the lines described in the following paper.

Experimental

2-1′-Hydroxyethyl-6-methoxynaphthalene.—A mixture of 2-acetyl-6-methoxynaphthalene (20 g.), aluminium *iso*propoxide (60 g.), and *iso*propyl alcohol was boiled under a fractionating column, with slow distillation until the distillate no longer gave a precipitate with 2 : 4-dinitrophenylhydrazine in aqueous acid. The mixture was then poured with stirring into excess of dilute hydrochloric acid containing ice, and the precipitate collected, washed, and dried (yield 16 g.). On recrystallisation light from petroleum (b. p. 80—100°)–benzene, *2-1′-hydroxyethyl-6-methoxynaphthalene* was obtained as colourless needles, m. p. 112° (Found : C, 77·6; H, 7·0. $C_{13}H_{14}O_2$ requires C, 77·2; H, 7·0%).

1 : 4-Dihydro-6-1′-hydroxyethyl-2-methoxynaphthalene (V).—2-1′-Hydroxyethyl-6-methoxynaphthalene (10 g.) in ethanol (100 ml.) was added with vigorous stirring, followed by thin slices of sodium (1·8 g.), to liquid ammonia (500 ml.). Then the mixture was poured into water (500 ml.) and extracted with ether, and the extracts were dried and evaporated. The residue (8 g.), on recrystallisation from light petroleum (b. p. 60—80°), gave *1 : 4-dihydro-6-1′-hydroxyethyl-2-methoxynaphthalene* as plates, m. p. 87° (Found : C, 76·5; H, 7·5. $C_{13}H_{16}O_2$ requires C, 76·4; H, 7·8%).

For the hydrolysis 5 g. of the enol ether were shaken with 10% hydrochloric acid (100 ml.) at 40° for 1 hr., and the product extracted with ether. The residue on drying and evaporation of the ether was distilled (b. p. 116°/0·05 mm.) (Found : C, 81·2; H, 7·6. $C_{13}H_{14}O_2$ requires C, 80·0; H, 7·8. $C_{13}H_{12}O$ requires C, 83·6; H, 7·0%). It had a CO absorption band at 5·84 μ, and gave a yellow oily dinitrophenylhydrazone.

6-Ethyl-1 : 2 : 3 : 4 : 5 : 8-hexahydro-2-oxonaphthalene (IV).—2-1′-Hydroxyethyl-6-methoxynaphthalene (10 g.) was reduced as above with sodium (5·8 g.), liquid ammonia (350 ml.), and ethanol (100 ml.), the product isolated with ether, the ether evaporated, and the residue warmed for 30 min. with ethanol (25 ml.) and 10% hydrochloric acid (25 ml.). The mixture was poured into water, and the oil extracted with ether. After evaporation of the ether the residual oil was distilled, giving *6-ethyl-1 : 2 : 3 : 4 : 5 : 8-hexahydro-2-oxonaphthalene*, b. p. 162°/17 mm. (Found : C, 81·2; H, 9·1. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%). It had a CO absorption band at 5·85 μ and gave a yellow oily dinitrophenylhydrazone that became red in hot alcoholic sulphuric acid.

Ethyl 6-Methoxy-5-methyl-2-naphthoate.—6-Methoxy-5-methyl-2-naphthoic acid (12 g.), ethanol (200 ml.), and concentrated sulphuric acid (5 ml.) were boiled under reflux for 10 hr., then poured into water, and the *ester* was isolated by ether-extraction. It formed plates, m. p. 99—100°, from ethanol (Found : C, 73·6; H, 6·6. $C_{15}H_{16}O_3$ requires C, 73·6; H, 6·55%).

1 : 2 : 3 : 4-Tetrahydro-2-hydroxymethyl-6-methoxy-5-methylnaphthalene (VIII).—Sodium (9·5 g.) was added in thin slices to a solution of ethyl 6-methoxy-5-methyl-2-naphthoate (10 g.) in liquid ammonia (500 ml.) and dry ethanol (150 ml.). The solution rapidly became yellow. When the sodium had dissolved the mixture was poured into water (500 ml.), and the product extracted with ether. Removal of the ether and recrystallisation of the residue from light petroleum (b. p. 60—80°) gave *2-hydroxymethyl-5-methyl-1 : 2 : 3 : 4-tetrahydronaphthalene*, prisms, m. p. 87° (Found : C, 75·4; H, 8·7. $C_{12}H_{16}O_2$ requires C, 75·6; H, 8·7%), which showed no CO band in the infrared region, but a OH band at 3·05 μ. This substance was recovered unchanged after prolonged boiling with alcoholic sodium hydroxide, and gave no trace of ketonic material on prolonged boiling with dilute hydrochloric acid.

6-(1-Ethyl-3-hydroxy-2 : 2-dimethyl)propyl-1 : 2 : 3 : 4-tetrahydro-2-oxonaphthalene (XI).—Ethyl 3-hydroxy-3-6′-methoxynaphthyl-2 : 2-dimethylpentanoate (X) (25 g.) in dry ethanol (150 ml.) was added, followed by sodium (14·5 g.), to liquid ammonia (750 ml.) with vigorous stirring. After the reduction the mixture was poured into water, the product extracted with ether, the extract evaporated, and the residue warmed at 50° for 30 min. with 10% alcoholic hydrochloric acid. This mixture was poured into water, the product extracted with ether, and the ether evaporated. The residue was then boiled under reflux with methanol (200 ml.), acetic acid (10 ml.), and Girard's reagent P (25 g.) for 2 hr., the mixture poured into dilute sodium hydroxide solution until the mixture was just alkaline to litmus, the non-ketonic matter removed by four extractions with ether, and the aqueous solution heated on the water-bath for 1½ hr. after acidification with hydrochloric acid. The mixture was finally cooled, and the product extracted with ether. The ether extracts on evaporation afforded a dark brown oil that was purified by distillation, giving pale brown *hydroxy-ketone* (2·5 g.), b. p. 180°/0·03 mm. (Found : C, 78·6; H, 9·6. $C_{17}H_{24}O_2$ requires C, 78·4; H, 9·3%).

Condensation of the Ester (X) *with Methylmagnesium Iodide.*—The ester (25 g.) and excess of methylmagnesium iodide (from 10 g. of magnesium) were heated in benzene (190 ml.)–ether

(40 ml.) for 8 hr., the mixture was cooled and acidified with ice and hydrochloric acid, and the benzene layer separated. Drying of the benzene solution, evaporation, and recrystallisation from light petroleum (b. p. 40—60°) and from ethanol gave a mixture as prisms, m. p. 87° (Found : C, 84·4; H, 7·6. Calc. for $C_{20}H_{26}O_2$: C, 80·5; H, 8·7. Calc. for $C_{20}H_{24}O$: C, 85·6; H, 8·6%).

When this product was reduced by sodium and liquid ammonia and the product distilled, visible dehydration and decomposition rapidly took place.

2-(2-*Hydroxy*-2-*methylpropyl*)-3-(6-*methoxy*-2-*naphthyl*)-1-*methyl*cyclo*pentanol* (XIV; R = Me).—Ethyl 2-(6-methoxy-2-naphthyl)-5-oxo*cyclo*pentyl acetate (10 g.) and excess of methylmagnesium iodide were heated under reflux in ether (250 ml.) for 5 hr., the mixture was decomposed by ice and hydrochloric acid, and the ether layer removed. The ether solution after drying and evaporation yielded a viscous oil that partly crystallised. This was shaken with benzene, and the solid was collected and recrystallised from methanol yielding 2-(2-*hydroxy*-2-*methylpropyl*)-3-(6-*methoxy*-2-*naphthyl*)-1-*methyl*cyclo*pentanol* as prisms, m. p. 147° (Found : C, 76·5; H, 8·8. $C_{21}H_{28}O_2$ requires C, 76·7; H, 8·5%). The benzene solution, on evaporation and distillation, yielded a pale brown *substance*, b. p. 160°/0·024 mm. (Found : C, 81·8; H, 8·5. $C_{21}H_{26}O_2$ requires C, 81·4; H, 8·4%), evidently a monodehydrated derivative of (XIV; R = Me).

2-2′-*Hydroxyethyl*-3-(6-*methoxy*-2-*naphthyl*)cyclo*pentanol* (XIV; R = H).—Ethyl 2-(6-methoxy-2-naphthyl)-6-oxo*cyclo*pentylacetate (15 g.) and excess of lithium aluminium hydride were heated under reflux in dry ether for 1 hr., the mixture was decomposed by dilute hydrochloric acid, and the ether layer evaporated, affording crystals that, recrystallised from benzene–light petroleum (b. p. 60—80°), gave 2-2′-*hydroxyethyl*-3-(6-*methoxy*-2-*naphthyl*)cyclo*pentanol*, prisms (12 g.), m. p. 130° (Found : C, 75·5; H, 7·7. $C_{18}H_{22}O_2$ requires C, 75·5; H, 7·7%).

2-(2-*Hydroxy*-2-*methylpropyl*)-3-(5 : 6 : 7 : 8-*tetrahydro*-6-*oxo*-2-*naphthyl*)-1-*methyl*cyclo*pentanol* (XVI; R = Me).—The alcohol (XIV; R = Me) (10 g.) was reduced with sodium (4 g.), liquid ammonia (400 ml.), and ethanol (150 ml.), and the product isolated with ether. The ether extract was shaken for 5 hr. with dilute hydrochloric acid, washed with water, and dried. On evaporation the residue crystallised in part and was shaken with light petroleum (b. p. 40—60°), and the solid collected and recrystallised from benzene–light petroleum (b. p. 60—80°), giving the *keto-alcohol* as prisms, m. p. 133—134° (Found : C, 75·9; H, 8·9. $C_{20}H_{28}O_2$ requires C, 75·9; H, 8·9%). This had a CO absorption band at 5·82 μ and a OH band at 3·1 μ.

The extract obtained by shaking the crude product with light petroleum was evaporated to dryness and the viscous residue distilled. 2-(2-*Hydroxy*-2-*methylpropyl*)-3-(1 : 4 : 5 : 6 : 7 : 8-*hexahydro*-6-*oxo*-2-*naphthyl*)-1-*methyl*cyclo*pentanol* (XVII) was obtained as a very pale brown oil, b. p. 210°/0·05 mm. (Found : C, 75·1; H, 9·1. $C_{20}H_{30}O_2$ requires C, 75·4; H, 9·4%).

2-2′-*Hydroxyethyl*-3-(5 : 6 : 7 : 8-*tetrahydro*-6-*oxo*-2-*naphthyl*)cyclo*pentanol* (XVI; R = H).—The ketone (XIV; R = H) (10 g.) was reduced with sodium (3 g.), ammonia (250 ml.), and ethanol (250 ml.), and the product isolated as before. After hydrolysis of the extract by shaking it with hydrochloric acid for 5 hr. and distillation, the 3-*hydroxy*-*ketone* was obtained as an almost colourless oil, b. p. 185—190°/0·05 mm. (Found : C, 75·3; H, 7·9. $C_{17}H_{22}O_2$ requires C, 74·8; H, 7·9%).

6 : 6′-*Dihydroxy*-2 : 2′-*dinaphthyl* (XVIII; R = H).—6-Bromo-2-naphthol (10 g.), a 5% 2-ethoxyethanol solution of potassium hydroxide (100 ml.), and 4% palladised strontium carbonate (5 g.) were heated at 135—140° under reflux with vigorous stirring, and 100% hydrazine hydrate (1·2 g.) was added. The mixture was boiled under reflux for 1 hr., cooled, filtered, acidified with hydrochloric acid, heated to the b. p., and diluted with water to incipient precipitation, then allowed to cool. 6 : 6′-*Dihydroxy*-2 : 2′-*dinaphthyl* separated as pale brown plates, which recrystallised from a large volume of 2-ethoxyethanol as fawn-coloured plates, m. p. 297—298° (Found : C, 83·4; H, 4·9. $C_{20}H_{14}O_2$ requires C, 83·8; H, 4·9%), readily soluble in alkalis and giving a green colour with ferric chloride.

6 : 6′-*Dimethoxy*-2 : 2′-*dinaphthyl* (XVIII; R = Me).—6-Bromo-2-methoxynaphthalene (10 g.) was reduced with hydrazine hydrate (1·2 g.; 100%), 5% 2-ethoxyethanolic potassium hydroxide (100 ml.), and palladised strontium carbonate (5 g.) as above. The solid matter was collected and boiled with nitrobenzene (50 ml.), and the solution filtered whilst hot. The filtrate on cooling deposited a quantity of almost colourless 6 : 6′-*dimethoxy*-2 : 2′-*dinaphthyl* (0·9 g.), plates, m. p. 289° (from nitrobenzene) (Found : C, 83·3; H, 6·0. $C_{22}H_{18}O_2$ requires C, 83·0; H, 5·8%), very sparingly soluble in the usual solvents.

6 : 6′-*Di*-(2-*hydroxyethoxy*)-2 : 2′-*dinaphthyl* (XVIII; R = $CH_2{\cdot}CH_2{\cdot}OH$).—2-Bromo-6-2′-hydroxyethoxynaphthalene (see below) (10 g.) was reduced as above. The solid deposited from

the mixture on cooling was extracted with boiling ethylene chlorohydrin; **6 : 6'-*di*-(2-*hydroxyethoxy*)-2-2'-*dinaphthyl*** separated from the filtrate and formed plates, m. p. 280°, on recrystallisation from ethylene chlorohydrin (Found: C, 77·5; H, 6·2. $C_{24}H_{22}O_4$ requires C, 77·0; H, 5·9%).

6 : 6'-*Di*-(2 : 3-*dihydroxypropoxy*)-2 : 2'-*dinaphthyl* [XVIII; R = CH_2·CH(OH)·CH_2·OH)].—6 : 6'-Dihydroxy-2 : 2'-dinaphthyl (10 g.) was dissolved in alkali and heated on the water-bath with glycerol α-chlorohydrin (10 g.) until no further precipitate was formed. The crystalline solid was then collected and a sample recrystallised from diethylene glycol, giving the *ether* as plates (10 g.), m. p. 319° (Found: C, 71·4; H, 6·0. $C_{26}H_{26}O_6$ requires C, 71·8; H, 5·9%).

Reduction. The ether (10 g.) in hot triethylene glycol (400 ml.) was added slowly to a solution of sodium (25 g.) in liquid ammonia (1·5 l.) with vigorous stirring. When all the sodium had reacted the mixture was poured into water (2 l.), and the solid collected and shaken with ethyl acetate (150 ml.) and 2N-hydrochloric acid (200 ml.) until no further diminution in the amount of undissolved solid was noticed. The ethyl acetate layer was separated, washed with water, dried, and evaporated. The residue failed to crystallise, was dissolved in ethyl acetate, and passed through a column of activated alumina. The eluate from the column yielded 1·5 g. of a brown oil that was distilled, giving a pale brown oily *diketone* (? XX), b. p. 250°/0·001 mm. (Found: C, 81·1; H, 8·6. $C_{26}H_{24}O_2$ requires C, 81·1; H, 8·1%). This substance gave a red 2 : 4-dinitrophenylhydrazone that could not be purified.

2-Bromo-6-2'-hydroxyethoxynaphthalene.—6-Bromo-2-naphthol (10 g.) was heated on the water-bath with 10% aqueous potassium hydroxide (50 ml.) and ethylene chlorohydrin (10 g.) for 1 hr., then cooled. The *ether* was obtained as plates, m. p. 110°, from 60% acetic acid (Found: C, 56·2; H, 4·5; Br, 30·0. $C_{12}H_{11}OBr,H_2O$ requires C, 56·6; H, 4·9; Br, 30·4%).

Reduction. This ether (10 g.) was reduced with sodium (5 g.), liquid ammonia (400 ml.) and ethanol (50 ml.). The product was isolated by ether-extraction and hydrolysed with dilute hydrochloric acid and ethanol. The product was β-tetralone, which was purified by distillation (b. p. 135°/15 mm.) (Found: C, 81·6; H, 7·2; Br, 0·0. Calc. for $C_{10}H_{10}O$: C, 82·0; H, 6·9%).

Reduction of 6-Acetyl-1-chloro-2-methoxynaphthalene.—6-Acetyl-1-chloro-2-methoxynaphthalene (20 g.) was reduced by sodium (18 g.), liquid ammonia (600 ml.), and ethanol (100 ml.), and the product hydrolysed with alcoholic hydrochloric acid to an amber-coloured oil that was purified by distillation. 6-Ethyl-1 : 2 : 3 : 4 : 5 : 8-hexahydro-2-oxonaphthalene was obtained as colourless oil, b. p. 160°/17 mm. (Found: C, 80·9; H, 8·9. Calc. for $C_{12}H_{16}O$: C, 81·8; H, 9·1%).

3 : 4-*Di*-(6-*methoxy*-2-*naphthyl*)*hexane*-3 : 4-*diol* (XXI).—2-Methoxy-6-propionylnaphthalene (10 g.), absolute ethanol (100 ml.), dry sulphur-free benzene (75 ml.), freshly scoured aluminium foil (6 g.), and powdered mercuric chloride (0·25 g.) were heated on a water-bath for 15 hr.; by then all the aluminium had dissolved. The mixture was cooled, acidified with excess of ice-cold hydrochloric acid, and extracted with ether. The extract afforded, on evaporation, a brown gum, which was triturated with dilute acetic acid. Solid which separated was collected (1·1 g.) and recrystallised from 2-ethoxyethanol, giving the *diol* as prisms, m. p. 205° (Found: C, 78·3; H, 7·0. $C_{28}H_{30}O_4$ requires C, 78·1; H, 7·0%). Dehydration of this pinacol with acetic anhydride and acetyl chloride yielded intractable products.

2-1'-Hydroxypropyl-6-methoxynaphthalene.—2-Methoxy-6-propionylnaphthalene (25 g.) was heated with aluminium *iso*propoxide (25 g.) and *iso*propyl alcohol (250 ml.) with slow distillation, until the distillate no longer contained acetone. The mixture was then poured with stirring into ice and hydrochloric acid, and the precipitate collected and recrystallised from benzene–light petroleum (b. p. 60—80°); ***2-1'-hydroxypropyl-6-methoxynaphthalene*** was obtained as plates, m. p. 87° (Found: C, 77·5; H, 7·6. $C_{14}H_{16}O_2$ requires C, 77·8; H, 7·4%). The *acetate*, prepared by refluxing acetic anhydride, formed plates, m. p. 65°, from light petroleum (b. p. 60—80°) (Found: C, 75·1; H, 7·3. $C_{16}H_{18}O_3$ requires C, 74·3; H, 7·0%).

Attempts to dehydrate the alcohol by heating it with formic acid, iodine, or anhydrous cupric sulphate gave only polymerised compounds.

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*The Synthesis of Potential Androgens. Part II.**

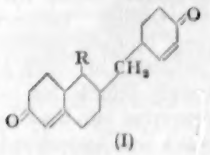
By K. W. Bentley and W. C. Firth.

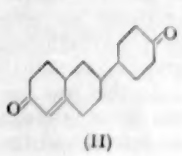
[Reprint Order No. 6055.]

Substances bearing a superficial resemblance to testosterone have been synthesised for androgenic testing. In addition anisoin and anisil have been submitted to the sodium and liquid ammonia reduction.

Following from the work described in Part I * it was decided to prepare several diketones of the general type (I), which are dehydrogenated homologues of the compound (II) reported by Wilds and Shunk (*J. Amer. Chem. Soc.*, 1949, **71**, 3266) to be feebly androgenic.

Condensation of 6-methoxy-1-tetralone with *p*-methoxybenzaldehyde gave a good yield of the αβ-unsaturated ketone, which was catalytically reduced to the benzyl compound (III). Clemmensen reduction of the latter failed, but reduction by Huang-Minlon's method afforded the ether (IV; R = H). This was sparingly soluble in a mixture of liquid ammonia and ethanol, but reduction was effected under the conditions found to be the most suitable for this type of reaction, *viz.*, by using an approximately 50% mixture of liquid ammonia and ethanol; in this mixture sodium does not dissolve to give a blue solution, nor does it remain solid metal, as when it is added to ethanol; instead, a copper-coloured molten mass is formed, and this dissolves slowly and quietly as the reduction proceeds. The yields by this technique were greatly superior to those obtained by using less alcohol. In this way the benzyl compound (IV; R = H) was reduced to a compound that on hydrolysis yielded the αβ-unsaturated ketone (I; R = H) (the intermediate βγ-unsaturated ketone was not isolated).


(I)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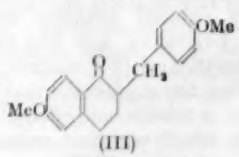
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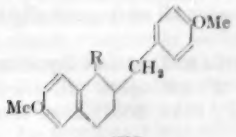
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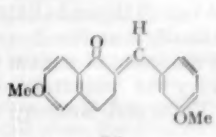
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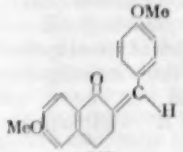
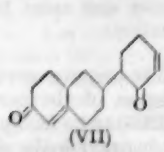

(VI)

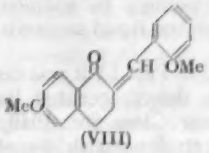
Repetition of this series of reactions with *m*-methoxybenzaldehyde afforded, on two different occasions, two different αβ-unsaturated ketones in the first step. These were shown to be chemical individuals not polymorphs and must be *cis–trans*-isomers: in agreement, both substances yielded the same dihydro-derivative on catalytic hydrogenation. The αβ-unsaturated ketones produced in the initial condensations of 6-methoxy-1-tetralone with *o*-, *m*-, and *p*-methoxybenzaldehyde form 2 : 4-dinitrophenylhydrazones only with difficulty, whereas the reduced ketones form these derivatives with ease. It is suggested that this difficulty of hydrazone formation in the unsaturated bodies is a result of steric hindrance, and that these compounds have the *cis*-configuration as in (VI). Of the two isomers obtained in the *m*-methoxy-series that formed as in the *o*- and *p*-series by allowing the reaction mixture to cool until separation of the ketone occurs is presumably the *cis*-form analogous to (VI), whilst the isomer obtained by pouring the mixture into water and isolating and distilling the product probably has the *trans*-configuration (V).

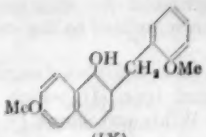
* Part I, preceding paper.

Insufficient quantities of *m*-methoxybenzaldehyde were available to permit extension of this series of reactions beyond the dihydro-derivative of (V).

The sequence of reactions was carried through with *o*-methoxybenzaldehyde to the diketone (VII). An attempt to reduce the double bond of the benzylidene-ketone (VIII) and the carbonyl group (to CH_2) in one reaction catalytically in acetic acid and perchloric acid over palladised charcoal (cf. Rosenmund and King, *Ber.*, **1942**, **75**, 1850; Hornung and Reisner, *J. Amer. Chem. Soc.*, **1948**, **70**, 3619; **1949**, **71**, 1036) gave only the saturated alcohol (IX).


(VII)


(VIII)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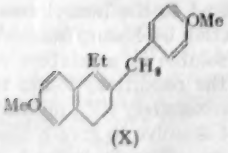
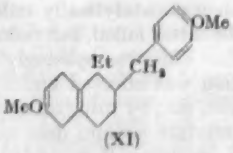
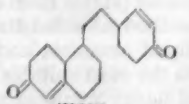

(X)


(XI)

(XII)

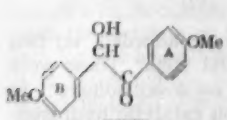

(XIII)

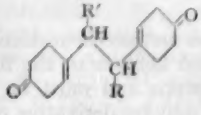
Condensation of (III) with ethylmagnesium iodide and dehydration of the product by distillation afforded 1-ethyl-3 : 4-dihydro-6-methoxy-2-4′-methoxybenzylnaphthalene (X), hydrogenation of which yielded the ether (IV; R = Et). Reduction of the latter with sodium, ammonia, and ethanol under the conditions outlined above gave excellent yields of the enol ether (XI), and thence by hydrolysis the αβ-unsaturated diketone (I; R = Et).

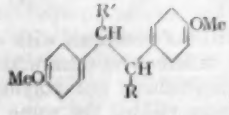
As the diphenol (XII) is oestrogenic (Buchta, Galster, and Dauner, *Chem. Ber.*, 1949, **82**, 207) a reduced analogue was prepared for androgenic testing. Interaction of 6-methoxy-1-tetralone and 2-(*p*-methoxyphenyl)ethylmagnesium bromide afforded 3 : 4-dihydro-4-methoxy-1-(2-4′-methoxyphenylethyl)naphthalene, reduction of which gave the corresponding tetrahydronaphthalene. As this was too sparingly soluble for reduction with sodium, ammonia, and ethanol, it was demethylated and converted into the 2-hydroxyethyl ether, which was then reduced as before, and the product was hydrolysed to the αβ-unsaturated ketone (XIII).

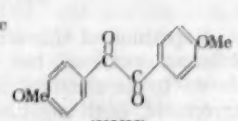
The compounds (I; R = H and Et), (VII), and (XIII) were all androgenically inactive, and this series of investigations was finally abandoned.

During these investigations the reduction of anisoin with sodium and liquid ammonia was carried out as a preliminary to preparation of analogues of the hexane (XV; R = R′ = Et) obtained by Birch and Mukherji (*J.*, 1949, 2531) from hexoestrol.


(XIV)

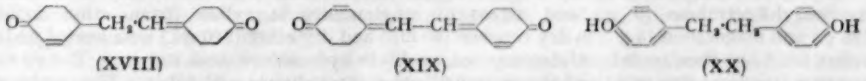

(XV)


(XVI)


(XVII)

The reduction proceeded readily and gave two substances (XVI; R = OH, R′ = H; R = R′ = H). These probably arise as follows. The nucleus A of anisoin (XIV) having a CO substituent would be rapidly reduced, whereas nucleus B would be reduced more slowly, and indeed the hydrogenolysis of the benzyl-alcoholic hydroxyl group must precede the reduction of B. The reduction of the carbonyl group will compete with the reduction of nucleus A as the first process, and when this reduction precedes nuclear reduction both rings will become identical and elimination of both central oxygen functions will occur; when, however, nuclear reduction precedes reduction of the carbonyl group the reduction of the latter will not give a benzyl alcohol and retention of the alcoholic OH group would

be expected, giving (XVI; R = OH, R′ = H). As expected from this theory, anisil (XVII), when reduced in the same way, gave the diol (XVI; R = R′ = OH).



(XVIII) (XIX) (XX)

The hydrolysis of these derivatives of anisoin and anisil gave rise to interesting compounds. The hydrolysis of the alcohol (XVI; R = OH, R′ = H) apparently involves simultaneous dehydration, presumably giving the conjugated unsaturated ketone (XVIII). Double dehydration also appears to accompany the hydrolysis of the diol (XVI; R = R′ = OH), giving the highly unsaturated ketone (XIX). The isomeric dihydroxydiphenylethane structure (XX) for this substance was eliminated by the melting point, the ultraviolet absorption spectrum, and the formation of a 2 : 4-dinitrophenylhydrazone. The ketone rapidly degenerates into tars.

Experimental

1 : 2 : 3 : 4-*Tetrahydro-6-methoxy-2-4′-methoxybenzylidene*-1-*oxonaphthalene*.—A solution of sodium (2 g.) in ethanol (50 ml.) was added to one of 6-methoxy-1-tetralone (15 g.) and *p*-methoxybenzaldehyde (18 g.) in ethanol (100 ml.) at 75° in a 200-ml. flask with exclusion of air. On slow cooling, pale yellow plates separated. These were collected, washed with cold ethanol, and recrystallised from 500 ml. of ethanol, yielding the ***methoxybenzylidene derivative*** as pale yellow, irregular plates, m. p. 139·5° (Found: C, 77·4; H, 6·1. $C_{19}H_{18}O_3$ requires C, 77·5; H, 6·1%), which gave a 2 : 4-dinitrophenylhydrazone only with great difficulty.

1 : 2 : 3 : 4-*Tetrahydro-6-methoxy-2-4′-methoxybenzyl*-1-*oxonaphthalene*.—The foregoing product (15 g.) in purified dioxan (170 ml.) was shaken under hydrogen in the presence of palladised strontium carbonate. Hydrogen was steadily absorbed and reaction was stopped when one mol. had been absorbed (1143 ml. at N.T.P.). The catalyst was removed and the mixture concentrated under reduced pressure and poured into water. An oil which separated solidified and recrystallised from ethanol, giving the *benzyl compound* as prisms, m. p. 94° (Found: C, 76·7; H, 6·6. $C_{19}H_{20}O_3$ requires C, 77·0; H, 6·7%). The 2 : 4-*dinitrophenylhydrazone* formed dark red needles, m. p. 210°, from Cellosolve (2-ethoxyethanol) (Found: C, 63·0; H, 4·9; N, 11·7. $C_{25}H_{24}O_6N_4$ requires C, 63·2; H, 5·0; N, 11·7%).

1 : 2 : 3 : 4-*Tetrahydro-6-methoxy-2-4′-methoxybenzylnaphthalene*.—(*a*) 1 : 2 : 3 : 4-Tetrahydro-6-methoxy-2-4′-methoxybenzyl-1-oxonaphthalene (10 g.) was recovered after 48 hours' boiling with toluene (100 ml.), amalgamated zinc (100 g.), and concentrated hydrochloric acid (350 ml.), almost completely unchanged. (*b*) 1 : 2 : 3 : 4-Tetrahydro-6-methoxy-2-4′-methoxybenzyl-1-oxonaphthalene (15 g.) and 100% hydrazine hydrate (5 ml.) were boiled with a solution of sodium (5 g.) in diethylene glycol (150 ml.) for 1 hr. Water was then allowed to distil until the b. p. reached 200°, and the mixture was boiled under reflux, in an atmosphere of nitrogen, for 6 hr. No precipitate was obtained when the mixture was poured into water (500 ml.), so the phenol was remethylated immediately by the addition of sodium hydroxide (20 g.) and, slowly, methyl sulphate (50 ml.), with stirring and heating. Cooling, dilution with water (750 ml.), ether-extraction, evaporation, and distillation gave 1 : 2 : 3 : 4-*tetrahydro-6-methoxy-2-4′-methoxybenzylnaphthalene*, b. p. 185°/0·2 mm. (Found: C, 81·1; H, 8·1. $C_{19}H_{22}O_2$ requires C, 80·8; H, 7·8%). This compound was non-ketonic and non-phenolic.

1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*Octahydro-6-oxo-2-(4-oxocyclohex-2-enylmethyl)naphthalene*.—1 : 2 : 3 : 4-Tetrahydro-6-methoxy-2-4′-methoxybenzylnaphthalene (15 g.) in ethanol (500 ml.) was added, followed by sodium (20 g.) in slices, to liquid ammonia (500 ml.), with vigorous stirring until dissolution of the sodium was complete, then the whole was poured into water (1000 ml.) and extracted with ether, and the extracts were evaporated. The residual oil was warmed at 40° with alcoholic 2N-hydrochloric acid for 10 min., and the mixture poured into water and extracted with ether. The ether extract was shaken for 10 hr. with saturated aqueous sodium hydrogen sulphite, and the bisulphite compound collected and washed with ether. The ketone recovered from the bisulphite compound by decomposition and extraction with ether was heated at 50° for 5 min. with alcoholic sodium ethoxide in an atmosphere of nitrogen, the solution poured into dilute acetic acid, and the precipitated oil extracted with ether, which afforded 1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*octahydro-6-oxo-2-(4-oxocyclohex-2-enylmethyl)naphthalene*

(I; R = H) as a pale brown oil, b. p. 180°/0·05 mm. (Found: C, 70·5; H, 8·7. $C_{17}H_{22}O_2$ requires C, 79·0; H, 8·5%), $\lambda_{max.}$ 2280 Å (ε 10,000).

1-*Ethyl*-3 : 4-*dihydro*-6-*methoxy*-2-4′-*methoxybenzylnaphthalene* (X).—6-Methoxy-2-4′-methoxybenzyl-1-tetralone (9 g.) and excess of ethylmagnesium iodide [from ethyl iodide (28 g.) and magnesium (5 g.)] in dry benzene (60 ml.) and dry ether (240 ml.) were heated under reflux for 5 hr., then cooled and decomposed by dilute hydrochloric acid and ice. The ether–benzene layer was separated and the aqueous layer extracted once with ether. The combined extracts were shaken with sulphurous acid, then with sodium hydrogen carbonate solution, dried, and evaporated. The residual oil was distilled, to give a pale yellow oil, b. p. 193—195°/0·07 mm., which solidified. On low-temperature recrystallisation from ether 1-*ethyl*-3 : 4-*dihydro*-6-*methoxy*-2-4′-*methoxybenzylnaphthalene* was obtained as needles or prisms, m. p. 49—50° (Found: C, 82·0; H, 7·6. $C_{21}H_{24}O_2$ requires C, 81·8; H, 7·6%).

1-*Ethyl*-1 : 2 : 3 : 4-*tetrahydro*-6-*methoxy*-2-4′-*methoxybenzylnaphthalene* (IV; R = Et).—A solution of the foregoing dihydronaphthalene (12 g.) in ethanol (200 ml.) was shaken under hydrogen at atmospheric pressure and 50° with palladised strontium carbonate. Absorption of hydrogen (870 ml.) ceased after 2 hr. The *tetrahydronaphthalene* was an almost colourless oil, b. p. 210—215°/0·1 mm. (Found: C, 81·4; H, 8·2. $C_{21}H_{26}O_2$ requires C, 81·3; H, 8·4%).

1-*Ethyl*-1 : 2 : 3 : 4 : 5 : 8-*hexahydro*-6-*methoxy*-2-(4-*methoxy*cyclo*hexa*-1 : 4-*dienylmethyl*)-*naphthalene* (XI).—The preceding product (10·5 g.) in 2-ethoxyethanol (75 ml.) and ethanol (75 ml.) was added to a well-stirred solution of sodium (3 g.) in liquid ammonia (600 ml.), then, gradually, more sodium (total 20 g.) and ethanol (total 500 ml.) until the sodium appeared as a copper-coloured molten mass on the surface of the liquid. Vigorous stirring was then continued until all the sodium had dissolved. The mixture was poured into water and extracted with ether. The extracts yielded an oil (8·5 g.) which when distilled gave the cyclo*hexadienyl compound*, b. p. 170—175/0·04 mm. (Found: C, 80·1; H, 9·6. $C_{21}H_{30}O_2$ requires C, 80·2; H, 9·6%).

1-*Ethyl*-1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*octahydro*-6-*oxo*-2-(4-*oxo*cyclo*hex*-2-*enylmethyl*)*naphthalene* (I; R = Et).—A solution of the preceding *cyclo*hexadienyl compound (1·5 g.) in ether (10 ml.) was shaken with 2N-hydrochloric acid (10 ml.) for 5 hr. The ether layer was separated and the aqueous layer saturated with ammonium chloride and extracted with ether. From the ether extracts an oil was obtained and distilled; pale yellow 1-*ethyl*-1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*octahydro*-6-*oxo*-2-(4-*oxo*cyclo*hex*-2-*enylmethyl*)*naphthalene* was obtained, having b. p. 165—170°/0·05 mm. (Found: C, 80·2; H, 9·0. $C_{19}H_{26}O_2$ requires C, 79·8; H, 9·1%), $\lambda_{max.}$ 2290 Å (ε 10,009).

6-*Methoxy*-2-2′-*methoxybenzylidene*-1-*tetralone*.—A solution of sodium (1 g.) in ethanol (30 ml.) was added to one of 6-methoxy-1-tetralone (15 g.) and *o*-methoxybenzaldehyde (18 g.) in ethanol (100 ml.) at 75°, with exclusion of air. After long storage crystals separated and on recrystallisation from ethanol gave 6-*methoxy*-2-2′-*methoxybenzylidene*-1-*tetralone* as pale yellow prisms, m. p. 87·5° (Found: C, 78·0; H, 6·2. $C_{19}H_{18}O_3$ requires C, 77·6; H, 6·1%). The 2 : 4-*dinitrophenylhydrazone* was formed very slowly on the water-bath, and formed bright red prisms, m. p. 182°, from 2-ethoxyethanol (Found: C, 62·8; H, 4·5; N, 11·0. $C_{25}H_{22}O_6N_4$ requires C, 63·2; H, 4·6; N, 11·8%).

6-*Methoxy*-2-2′-*methoxybenzyl*-1-*tetralone*.—A solution of the benzylidenetetralone (10 g.) in purified dioxan (170 ml.) was shaken under hydrogen over palladised strontium carbonate until absorption of hydrogen, at first steady, became markedly slower (762 ml. absorbed). Removal of the catalyst and most of the solvent, pouring into water (200 ml.), extraction with ether, distillation (b. p. 206—209°/0·1 mm.), and low-temperature recrystallisation from ether gave the 2-2′-*methoxybenzyl compound*, prisms, m. p. 68° (Found: C, 76·6; H, 6·5. $C_{19}H_{20}O_3$ requires C, 77·0; H, 6·7%). The 2 : 4-*dinitrophenylhydrazone*, formed fairly readily, was bright red prisms, m. p. 176° (from 2-ethoxyethanol) (Found: C, 63·2; H, 5·1; N, 11·9. $C_{25}H_{24}O_6N_4$ requires C, 63·1; H, 5·0; N, 11·8%).

6-*Methoxy*-2-2′-*methoxybenzyl*-1-*tetralol*.—A solution of the 2-2′-methoxybenzylidenetetralone (2 g.) in acetic acid (20 ml.) and 60% perchloric acid (1 ml.) containing palladised charcoal (0·6 g.) was shaken under hydrogen at atmospheric pressure and 55°. When 305 ml. hydrogen had been absorbed (*ca.* 5 hr.) the mixture was freed from catalyst, neutralised, and extracted with ether. The ether extracts yielded a yellow oil that crystallised on trituration with ether. Recrystallisation from ethanol gave the *tetralol*, pale brown prisms, m. p. 82° [Found: C, 76·3; H, 6·8%; *M* (Rast), 318. $C_{19}H_{22}O_3$ requires C, 76·5; 7·3%; *M*, 298].

1 : 2 : 3 : 4-*Tetrahydro*-6-*methoxy*-2-2′-*methoxybenzylnaphthalene*.—6-Methoxy-2-2′-methoxybenzyl-1-tetralone (10 g.) and 100% hydrazine hydrate (5 ml.) were added to a solution of sodium (2·5 g.) in diethylene glycol (75 ml.) and the mixture boiled for 1 hr. Then water was

distilled until the b. p. rose to 200°, whereafter the mixture was refluxed for a further 6 hr., poured into water, and methylated as described for the 4-methoxybenzyl isomer. The product was isolated by ether-extraction and distilled, giving **1 : 2 : 3 : 4-*tetrahydro*-6-*methoxy*-2-2′-*methoxybenzylnaphthalene***, almost colourless, b. p. 150—155°/0·02 mm. (Found : C, 80·8; H, 8·1. $C_{19}H_{22}O_2$ requires C, 80·8; H, 7·8%).

1 : 2 : 3 : 4 : 5 : 8-*Hexahydro*-6-*methoxy*-2-(2-*methoxy*cyclo*hexa*-1 : 4-*dienylmethyl*)*naphthalene*.—A solution of the 2-2′-methoxybenzyltetralin (8·5 g.) in ethanol (100 ml.) was added dropwise to a stirred solution of sodium (3 g.) in liquid ammonia (750 ml.), then more sodium (total 18 g.) and ethanol (total 600 ml.). After the sodium had dissolved, the mixture was poured into water. By means of ether, the cyclo*hexadienyl compound* (crude, 7 g.) was obtained as a pale yellow oil, b. p. 158—162°/0·02 mm. (Found : C, 80·0; H, 9·2. $C_{19}H_{24}O_2$ requires C, 79·7; H, 9·1%).

1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*Octahydro*-6-*oxo*-2-(2-*oxo*cyclo*hex*-3-*enylmethyl*)*naphthalene*.—A solution of the preceding product (2 g.) in ether (15 m.) was shaken with 2N-hydrochloric acid (25 ml.) for 5 hr. The ether layer was separated, and the aqueous layer saturated with ammonium chloride and extracted once with ether. The combined ether solutions yielded a pale yellow oil (1·4 g.), which was distilled; **1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*octahydro*-6-*oxo*-2-(2-*oxo*cyclo*hex*-3-*enylmethyl*)*naphthalene*** was obtained as an almost colourless oil, b. p. 140—144°/0·04 mm. (Found : C, 79·4; H, 8·9. $C_{17}H_{22}O_2$ requires C, 79·0; H, 8·5%), $\lambda_{max.}$ 2300 Å (ε 11,700).

6-*Methoxy*-2-3′-*methoxybenzylidene*-1-*tetralone*-A (*cis*?).—A solution of sodium (0·3 g.) in ethanol (10 ml.) was added to 6-methoxy-1-tetralone (5 g.) and *m*-methoxybenzaldehyde (6 g.) in boiling ethanol (35 ml.) with exclusion of air. A dark oil slowly separated. When poured into dilute acid the oil crystallised. When twice recrystallised from ethanol, **6-*methoxy*-2-3-*methoxybenzylidene*-1-*tetralone*-A** formed very pale yellow needles, m. p. 69° (Found : C, 78·0; H, 6·0. $C_{19}H_{18}O_3$ requires C, 77·5; H, 6·1%). This gave a 2 : 4-dinitrophenylhydrazone that was not obtained pure.

6-*Methoxy*-2-3′-*methoxybenzylidene*-1-*tetralone*-B (*trans*?)(V).—The preparation of the A-isomer was repeated, but the oil that separated was extracted with ether, the ether removed, and the residue distilled, giving a pale yellow oil. This was crystallised at −70° from ether, and on low-temperature crystallisation of the product **6-*methoxy*-2-3′-*methoxybenzylidene*-1-*tetralone*-B** was obtained as almost colourless needles, m. p. 57°. This m. p. could not be raised (mixed m. p. with A-isomer, 50°) (Found : C, 77·5; H, 6·2. $C_{19}H_{18}O_3$ requires C, 77·5; H, 6·1%). The 2 : 4-*dinitrophenylhydrazone* was formed very slowly on the water-bath, and was obtained as dark red prisms, m. p. 197—198°, from chloroform (Found : C, 63·6; H, 4·5; N, 12·4. $C_{25}H_{22}O_6N_4$ requires C, 63·3; H, 4·6; N, 11·8%).

6-*Methoxy*-2-3′-*methoxybenzyl*-1-*tetralone*.—This was prepared by reduction of the two preceding isomers as in the preparation of the 2- and the 4-methoxybenzyl isomer. It was obtained as almost colourless prisms, m. p. 56° (Found : C, 76·8; H, 6·5. $C_{19}H_{20}O_3$ requires C, 77·0; H, 6·7%).

3 : 4-*Dihydro*-6-*methoxy*-1-(2-p-*methoxyphenylethyl*)*naphthalene*.—6-Methoxy-1-tetralone (40 g.) in dry benzene (100 ml.) was added to a solution of 2-*p*-methoxyphenylethylmagnesium bromide (from magnesium, 5·65 g., and 2-*p*-methoxyphenylethyl bromide, 53 g.) in dry ether (300 ml.), and the resulting mixture boiled for 2 hr., then poured into excess of saturated aqueous ammonium chloride. Working up as above gave a viscous oil that was slowly distilled *in vacuo*. Dehydration occurred. The distillate solidified and was recrystallised from ethanol, yielding the *dihydronaphthalene*, plates, m. p. 84° (45 g.) (Found : C, 81·2; H, 7·3. $C_{20}H_{22}O_2$ requires C, 81·5; H, 7·5%).

1 : 2 : 3 : 4-*Tetrahydro*-6-*methoxy*-1-2′-p-*methoxyphenylethylnaphthalene*.—The dihydro-compound (40 g.) in ethanol (140 ml.) was shaken with palladised strontium carbonate under hydrogen at atmospheric pressure and 45° until absorption of hydrogen ceased. The solution was freed from catalyst and alcohol, giving the *tetrahydronaphthalene*, b. p. 185°/0·04 mm. (38 g.) (Found : C, 81·4; H, 8·2. $C_{20}H_{24}O_2$ requires C, 81·1; H, 8·1%).

1 : 2 : 3 : 4-*Tetrahydro*-6-*hydroxy*-1-2′-p-*hydroxyphenylethylnaphthalene*.—The preceding tetrahydronaphthalene (35 g.), glacial acetic acid (300 ml.), red phosphorus (2 g.), and concentrated hydriodic acid (200 ml.) were boiled together until evolution of methyl iodide ceased. The mixture was diluted with cold water (1 l.), and the precipitated oil extracted with ether. The ether extracts yielded a viscous oil that solidified on trituration with benzene. The solid, recrystallised from this solvent, gave the *phenol* as prisms, m. p. 95° (Found : C, 80·5; H, 7·5. $C_{18}H_{20}O_2$ requires C, 80·6; H, 7·5%), readily soluble in alkali and giving a green colour with ferric chloride.

1 : 2 : 3 : 4-*Tetrahydro-6-2′-hydroxyethoxy-2-2′-*(p-2-*hydroxyethoxyphenyl*)*ethylnaphthalene.***—The foregoing phenol (20 g.) in excess of aqueous sodium hydroxide was heated on the water-bath for 4 hr. with ethylene chlorohydrin (20 g.), the mixture allowed to cool, and the liquid decanted from the orange-yellow glass. The glass was taken up in chloroform, dried, recovered, and distilled. The *ether* was a pale yellow oil, b. p. 250—255°/0·04 mm. (18 g.) (Found : C, 74·9; H, 8·2. $C_{22}H_{26}O_4$ requires C, 74·3; H, 7·9%).

1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*Octahydro-6-oxo-*1-(2-4′-*oxo*cyclo*hex-*2′-*enylethyl*)*naphthalene.*—The ether (17 g.) was reduced with sodium (20 g.), liquid ammonia (750 ml.), and ethanol (600 ml.) by the method described above. The product was isolated in ether and shaken therein for 4 hr. with 2N-hydrochloric acid to ensure hydrolysis of the enol ether. The extracts were then washed, dried, and evaporated, leaving a brown oil that was purified by distillation. 1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*Octahydro-6-oxo-*1-(2-4′-*oxo*cyclo*hex-*2′-*enylethyl*)*naphthalene* was obtained as an almost colourless oil, b. p. 185—190°/0·05 mm. (Found : C, 79·4; H, 9·6. $C_{18}H_{24}O_2$ requires C, 79·2; H, 8·9%).

1 : 2-*Di-*(4-*methoxy*cyclo*hexa-*1 : 4-*dienyl*)*ethanol* (XVI; R = OH, R′ = H).—A warm solution of *p*-anisoin (15 g.) in ethanol (75 ml.) and 2-ethoxyethanol (75 ml.) was added, followed by sodium (27 g.), to liquid ammonia (750 ml.) with vigorous stirring. When all the sodium had dissolved the mixture was poured into water (2 l.) and extracted twice with ether. The combined extracts were washed, dried, and evaporated, leaving a yellow oil that solidified and recrystallised from ethanol; 1 : 2-*di-*(4-*methoxy*cyclo*hexa-*1 : 4-*dienyl*)*ethanol* was obtained as prisms (11 g. crude, 5·5 g. pure), m. p. 112—113°, mixed m. p. with anisoin (m. p. 113°) 98—99° (Found : C, 73·1; H, 8·1. $C_{14}H_{22}O_3$ requires C, 73·3; H, 8·4%).

1 : 2-*Di-*(4-*methoxy*cyclo*hexa-*1 : 4-*dienyl*)*ethane* (XVI; R = R′ = H).—The mother-liquors from the recrystallisation of crude 1 : 2-di-(4-methoxy*cyclo*hexa-1 : 4-dienyl)ethanol were evaporated and the residual brown tar was boiled under reflux with ether and animal charcoal for 30 min., then filtered off. The ether was removed, leaving a yellow oil that was distilled, giving very pale yellow 1 : 2-*di-*(4-*methoxy*cyclo*hexa-*1 : 4-*dienyl*)*ethane*, b. p. 133—136°/0·025 mm. (Found : C, 78·3; H, 9·0. $C_{14}H_{22}O_2$ requires C, 78·0; H, 8·9%).

1 : 2-*Di-*(4-*methoxy*cyclo*hexa-*1 : 4-*dienyl*)*ethane-*1 : 2-*diol* (XVI; R = R′ = OH).—*p*-Anisil (15 g.) in ethanol (110 ml.) and 2-ethoxyethanol (110 ml.) was added to liquid ammonia (750 ml.) with vigorous stirring, followed by sodium (15 g.). More sodium and ethanol were added as the reduction proceeded until a total of 30 g. of sodium and 500 ml. of ethanol had been added. Working up as usual and recrystallisation from ethanol afforded 1 : 2-*di-*(4-*methoxy*cyclo*hexa-*1 : 4-*dienyl*)*ethane-*1 : 2-*diol*, pale yellow prisms, m. p. 122·5° (Found : C, 69·5; H, 7·6. $C_{14}H_{22}O_4$ requires C, 69·1; H, 7·9%).

4-(2-4′-*Oxo*cyclo*hex-*2′-*enylethylidene*)cyclo*hex-*2-*enone** (XVIII).—1 : 2-Di-(4-methoxy*cyclo*hexa-1 : 4-dienyl)ethanol (2·4 g.) in ether (40 ml.) was shaken with 2N-hydrochloric acid (25 ml.) for 16 hr. The ether layer was separated, the aqueous layer saturated with ammonium chloride and extracted once with ether, the combined ether solutions were dried, and the ether was removed. The residual yellow oily *ketone* was distilled three times *in vacuo*, the final distillate solidifying (Found : C, 77·2; H, 7·7. $C_{14}H_{16}O_2$ requires C, 77·7; H, 7·4%).

*Glyoxylidenebis-*4-cyclo*hex-*2-*enone** (XIX).—A solution of 1 : 2-di-(4-methoxy*cyclo*hexa-1 : 4-dienyl)ethane-1 : 2-diol (1·5 g.) in chloroform (10 ml.) was shaken with 2N-hydrochloric acid (20 ml.) for 5 hr. The chloroform layer was separated, washed, dried, and evaporated, leaving a dark brown oil that solidified, giving, on recrystallisation from chloroform, *glyoxylidenebis-*4-cyclo*hex-*2-*enone* as irregular yellow plates, m. p. 207° (Found : C, 78·9; H, 6·5. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·5%), $\lambda_{max.}$ 3100 Å (ε 27,000) indicating a highly conjugated system.

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The Mechanism of a Chromate Process for the Separation of the Lanthanons and Yttrium.

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Lanthanon separations have been divided into two classes: those based on differences in solubility of salts, in which yttrium is interpolated in the heavy lanthanons between holmium and erbium, and those based on differences in basicity, in which it is interpolated in the middle lanthanons between gadolinium and terbium. From a mixture containing both middle and heavy lanthanons yttrium can be rapidly concentrated by a chromate process which combines both solubility and basicity separations in one operation; by the addition of a base to a lanthanon dichromate solution, the strongly basic lighter lanthanons are precipitated as double or normal chromates, while the weakly basic heavier lanthanons are removed by hydrolysis as basic salts.

Many procedures for the separation of the lanthanons and yttrium have been recommended, but the results could not be critically compared owing to the absence of reliable analyses. With the advent of spectrophotometry it is now possible to compare the various methods and to understand more fully the mechanisms involved. The aim of this investigation was to define a method for producing a fairly pure yttria from a material containing middle and heavy lanthanons. A number of procedures were compared involving fractional crystallization, precipitation, and decomposition, and it was found that the results could be grouped into three classes according to the mechanism involved, *i.e.*, separations achieved by differences in solubility of salts, by differences in basicity, and by the chromate procedure described below, the mechanism of which this paper is intended to clarify.

It is generally agreed that in separations based on differences in solubility of normal salts, whether by fractional crystallization of soluble salts, *e.g.*, bromates, or by fractional precipitation of sparingly soluble compounds, *e.g.*, double alkali sulphates, yttrium is interposed in the lanthanon sequence between holmium and erbium. The position of yttrium in a basicity separation is not satisfactorily established, however, the situation being undoubtedly complicated by the loose interpretation of the term basicity and the phenomena attributable to it. The situation has been reviewed by Moeller and Kremers (*Chem. Rev.*, **1945**, **37**, 97), who quote a number of different " orders of decreasing basicities " arrived at experimentally by various authors. The position of yttrium in the lanthanon sequence is reported as varying from between neodymium and samarium to between holmium and erbium, but in general is reported earlier in the sequence than for solubility separations.

Although chromate precipitation of the lanthanons has been much used for separating yttrium, no clear exposition of the mechanism has been given. Krüss and Loose (*Z. anorg. Chem.*, **1893**, **3**, 92) observed that didymium chromate could be precipitated by potassium chromate from a cold neutral nitrate solution of gadolinite earths, but a precipitate high in erbium was obtained on heating, and dichromate formation in the reaction liquor occurred. Britton (*J.*, **1924**, **125**, 1875) found that from 0·13M-solution only normal lanthanum and cerium chromates were precipitated, other lanthanon chromates being too soluble at pH values below the hydroxide precipitation figure to allow of solid normal chromate formation. However, by working with stronger solutions they appear to be obtainable. It is, moreover, evidently possible in the one reaction to obtain normal chromates of the strong bases and basic chromates of the weak bases. The majority of workers using the chromate process for separations adopted Muthmann and Böhm's technique (*Ber.*, **1900**, **33**, 42; *Z. angew. Chem.*, **1902**, **15**, 1282), that of slowly adding potassium chromate solution to a hot stirred dichromate solution of the lanthanons; a variant adopted for the present study was to cause precipitation by the addition of alkali instead of potassium chromate.

Experimental

Analysis.—All fractions were analyzed spectrophotometrically for certain lanthanons in neutral chloride solutions. Beer's law was found to hold adequately for dysprosium, holmium, erbium, thulium, and ytterbium, but not for gadolinium owing to incomplete resolution of its very sharp absorption bands, and a calibration curve was constructed from a pure gadolinium standard.

Starting Material.—Comparative runs were carried out on a crude yttrium oxide containing a high percentage of middle lanthanons, an analysis of which showed: Nd_2O_3, 0·1; Gd_2O_3, 19·7; Dy_2O_3, 16·0; Ho_2O_3, 2·2; Er_2O_3, 3·4; Y_2O_3, 58·6%. Light lanthanons, as shown by neodymium, were negligible, having been previously removed by double alkali sulphate precipitation; thulium and ytterbium were sought spectrophotometrically but not positively identified and were therefore of low order, and a small amount of terbium was indicated by the colour of the oxide; after analysis for gadolinium, dysprosium, holmium, and erbium, the rest was almost entirely yttrium which was estimated by difference, checked by occasional atomic-weight determinations.

Solubility Separations.—As an example of solubility separation, the fractional precipitation of the double alkali sulphates has been chosen for direct comparison with the chromate procedure. About 100 g. of oxide were converted into 1 l. of chloride solution and fractionally precipitated by slow addition of finely powdered anhydrous sodium sulphate to the cold stirred solution. Analyses of the oxides from the fractions obtained are shown in Table 1; the order

Table 1. *Composition (%) of oxides obtained from fractional precipitation of lanthanons with sodium sulphate.*

Fraction	% of Total Ln_2O_3 * removed	Composition (%)					
		Nd_2O_3	Gd_2O_3	Dy_2O_3	Ho_2O_3	Er_2O_3	Y_2O_3
1	13	1·2	56·2	15·2	1·1	1·9	24·4
2	23	0·2	38·0	20·4	1·8	2·2	37·4
3	13	—	19·5	24·3	2·5	3·0	50·7
4	15	—	6·9	21·0	3·0	3·9	65·2
5	8	—	1·0	17·7	3·1	4·5	73·7
Final liquor	28	—	—	6·0	2·1	4·9	87·0

* Including yttrium.

of precipitation is clearly Nd, Gd, (Tb), Dy, Ho, Y, and Er, the last two apparently coming out at about the same rate, although this point cannot be definitely established owing to the difficulty of accurate determination of the small percentage of erbium present and the inclusion of small amounts of other lanthanons in the yttrium figure. A good removal of middle lanthanons has been obtained, but erbium is concentrated with yttrium. The same order was shown by fractional crystallization of soluble salts, *e.g.*, nitrates.

Basicity Separations.—A number of these were examined, involving fractional precipitation by magnesia or ammonia at different concentrations, and fractional decomposition of the nitrates. The last is described here as an example of the type of results obtained. About 100 g. of oxide were converted into nitrate and fused until decomposition of the nitrate began; the melt was then held at 310° for 10 min., then poured rapidly into 700 ml. of cold water. Almost all the melt could be added before precipitation of the basic nitrate commenced; this was complete on storage overnight. The precipitate was filtered off (fraction A), the solution boiled down, and the fusion repeated at 10° intervals to yield further fractions. Analyses of the oxides from the fractions obtained are shown in Table 2. The order of precipitation is clearly

Table 2. *Composition (%) of oxides obtained from fractional decomposition of lanthanon nitrates.*

Fraction	% of total Ln_2O_3 * removed	Composition (%)					
		Nd_2O_3	Gd_2O_3	Dy_2O_3	Ho_2O_3	Er_2O_3	Y_2O_3
1	11	—	9·8	25·2	3·8	7·4	53·8
2	11	—	13·2	23·7	3·4	6·1	53·6
3	11	—	15·2	22·9	3·2	5·3	53·4
4	13	—	18·0	20·2	2·7	4·1	55·0
5	11	—	18·9	18·2	2·3	3·3	57·3
6	11	0·1	22·1	15·0	1·9	2·4	58·5
7	8	0·2	26·0	12·3	1·5	1·9	58·1
Final liquor	24	0·6	31·9	5·4	0·7	1·0	60·4

Er, Ho, Dy, Tb, Y, Gd, Nd (the position of terbium was shown by the colours of the oxides, which became progressively lighter). The identical order and a very similar degree of separation was shown by fractional precipitation by magnesia or ammonia.

Chromate Separations.—Earlier work in these laboratories on the use of the chromate procedure described below for the separation of the light lanthanons had already confirmed the formation of an insoluble double alkali chromate according to the equation

$$2Ln(NO_3)_3 + 2K_2Cr_2O_7 + 4KOH = K_2CrO_4.Ln_2(CrO_4)_3 + 6KNO_3 + 2H_2O$$

To 100 g. of oxide as nitrate solution were added 216 g. of potassium dichromate (the theoretical requirement of the above equation), and the mixture was made up to 1 l. The resulting solution was kept near the b. p. with continuous stirring while the material was precipitated fractionally by dropwise addition (1 hr.) of 125-ml. portions of 10% sodium hydroxide solution, followed by a further hour's digestion. The precipitates were filtered off, and converted into oxides

TABLE 3. *Composition (%) of oxides obtained from fractional precipitation of lanthanon chromates with sodium hydroxide.*

Fraction	% of total Ln_2O_3 * removed	Composition (%) Nd_2O_3	Gd_2O_3	Dy_2O_3	Ho_2O_3	Er_2O_3	Y_2O_3
1	20	0·9	39·9	27·0	2·6	3·6	26·0
2	24	0·2	29·4	24·0	2·9	4·2	39·3
3	21	—	21·2	16·3	2·8	4·5	55·2
4	19	—	9·1	6·5	1·8	3·2	79·4
5	14	—	—	1·3	0·5	1·3	96·9
Final liquor	2	—	—	0·4	0·2	0·4	99·0

via two oxalations. Analyses of the oxides from the fractions obtained are shown in Table 3. The order of precipitation is now Nd, Gd, (Tb), Dy, Ho, Er, Y, with erbium concentrating slightly initially, but being rapidly removed towards the end.

DISCUSSION

Although the results for solubility separations need little comment, confirming what has been reported previously, those for basicity separations warrant further investigation. The basicity procedures investigated, *viz.*, nitrate decomposition, and magnesia or ammonia precipitation at different concentrations, all agreed on the order of basicity as Nd, Gd, Y, Tb, Dy, Ho, Er; further, the degree of separation was similar for all, strongly suggesting that equilibria were approached between the lanthanons themselves irrespective of the

TABLE 4. *Composition (%) of oxides obtained by J. K. Marsh from fractional precipitation of weakly basic lanthanon chromates with sodium hydroxide.*

Fraction	% of total Ln_2O_3 * removed	Composition (%) Er_2O_3	Tm_2O_3	Yb_2O_3	Fraction	% of total Ln_2O_3 * removed	Composition (%) Er_2O_3	Tm_2O_3	Yb_2O_3
1	12	12	4·0	33	4	15	3·2	0·7	2·8
2	48	11	2·4	21	Final liquor	6	0·8	—	—
3	19	6·1	1·4	7·3					

* Including Y_2O_3.

means of precipitation. The results disagree with the majority of earlier reports on these techniques, which regard the basicity of yttrium as comparable with that of the light lanthanons, placing it between neodymium and samarium. They are, however, in agreement with the data on physicochemical investigations of equilibria between hydroxyl and lanthanon ions collected by Moeller and Kremers (*loc. cit.*) which place yttrium between gadolinium and erbium, lack of data excluding a more precise placing. These authors regard this as evidence in favour of their theoretically deduced basicity of yttrium between dysprosium and holmium, whereas the results above agree with Endres (quoted by Moeller and Kremers, *loc. cit.*) in placing it between gadolinium and dysprosium.

It is now obvious that the most convenient procedure for obtaining yttrium from a concentrate containing middle and heavy lanthanons requires two stages: a solubility

separation to remove the middle lanthanons and concentrate yttrium with the heavy lanthanons, followed by a basicity separation to remove the heavy lanthanons. The success of the chromate method is readily explained by assuming that these two requirements are met in one operation. In the presence of a high concentration of dichromate, initial addition of sodium hydroxide causes precipitation of the strong bases as double or normal chromates; as with the sodium sulphate precipitation, light lanthanons, gadolinium, terbium, and some dysprosium are removed, leaving yttrium and erbium in the liquor. As the pH and the dilution of the solution increase on further addition of sodium hydroxide, hydrolysis becomes increasingly effective and basic chromates of the weak bases are precipitated; the heavy lanthanons are removed, leaving yttrium in solution.

Support for this mechanism is given in a personal communication from J. K. Marsh, who found that application of a similar chromate procedure to a nitrate solution of weakly basic lanthanons, using sodium dichromate and sodium hydroxide, resulted in their precipitation in reverse order of basicity, *i.e.*, ytterbium, thulium, erbium; his results are given in Table 4. Further support is given by the nature of the precipitate, which, during the run shown in Table 3, changed from bright orange, dense, readily filterable crystals in the early fractions to a pale yellow flocculent hydrate-type material at the end. Moreover, although the equation given above obviously does not hold throughout the fractionation, when the potassium dichromate initially present was decreased to 75% of its requirement, or if the initial oxide concentration was reduced to 30 g./l., a considerably poorer separation of gadolinium and terbium resulted. Both alterations favour the basicity separation, and unless these two elements are removed during the initial solubility separation stage, they persist in the last fractions by reason of their comparatively high basicity.

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Indazole Derivatives: The Synthesis of Various Amino- and Hydroxy-indazoles and Derived Sulphonic Acids.

By ROBERT R. DAVIES.

[Reprint Order No. 6117.]

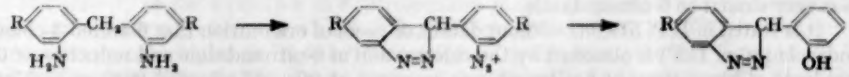
The preparation of a series of indazole derivatives from various substituted *o*-toluidines is described and evidence given that 3-nitro-2 : 6-xylidine affords a mixture of 6- (36%) and 4-nitro-7-methylindazole (64%). Chlorination of 6-nitroindazole affords 3-chloro-6-nitroindazole whereas sulphonation and nitration give the 5-substituted derivatives. Nitration and sulphonation of 5-nitroindazole give the 7-substituted derivatives.

The preparation and properties of several new amino- and hydroxy-indazolesulphonic acids * are described and tentative structures assigned to the products.

THE preparation of nitroindazoles from the corresponding nitro-*o*-toluidines and related compounds *via* their diazo-derivatives is well known (see, *e.g.*, Grandmougin, Noelting, and Witt, *Ber.*, 1890, **23**, 3655; Grandmougin and Michel, *Ber.*, 1893, **26**, 2349; Noelting, *Ber.*, 1904, **37**, 2556). The method for the preparation of 5-nitroindazole (*Org. Synth.*, **20**, 72) by interaction of 4-nitro-*o*-toluidine ($NH_2 = 1$) with sodium nitrite in acetic acid was found of general easy applicability. With a series of *o*-toluidines indazoles are formed in good yield if a nitro-group is present and earlier work by Duval (*Compt. rend.*, 1908,

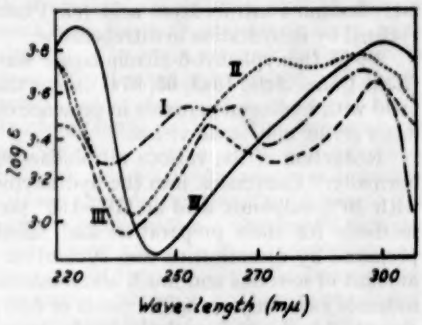
* Patent protection pending.

146, 1407; 1912, **154**, 780) on the ring closure of bis-*o*-aminophenylmethanes by tetrazotisation showed that electronegative groups in the *para*-position favoured ring closure. In the light of recent work and Duval's finding that his " bis-endo-azo compounds " gave a monohydroxy-compound on hydrolysis, it appears probable that his products were cyclised on one side.



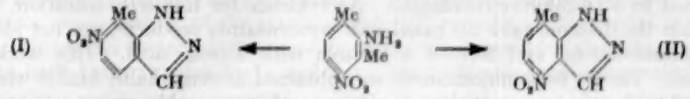
Although *o*-toluidine gives only 3—6% yields of indazole on reaction with nitrous acid (*Org. Synth.*, *loc. cit.*), Pschorr and Hope (*Ber.*, 1910, **43**, 2563) obtained a 75% yield of 3-cyanoindazole from 2-aminobenzyl cyanide. So, with electronegative substituents in the side chain and the nucleus, indazole formation might be expected to approach 100%. Conversely, chlorine or methyl in the 5-position depressed the yield.

Noelting (*Ber.*, 1904, **37**, 2556) stated that 3-nitro-2 : 6-xylidine gave two methylnitroindazoles, m. p. 175—176° and 222·5° respectively but did not assign structures. In our hands the reaction of 3-nitro-2 : 6-xylidine with nitrous acid in acetic acid gave 76% of mixed isomers, extraction of which with 50% alcohol afforded an insoluble isomer, m. p. 222° (64%), and a soluble isomer, m. p. 179° (36%). The former was 7-methyl-6- (I) and the latter 7-methyl-4-nitroindazole (II) since the amine derived from the latter coupled readily with diazo-compounds, as also did the derived hydroxyindazole, whereas the isomeric compounds did not. Further, the 2 : 3-hydroxynaphthoylamide derived from the



Absorption spectra for (I) *1-methylindazole*, (II) *2-methylindazole*, (III) *7-hydroxy-1-methylindazole*, *and* (IV) *7-hydroxy-2-methylindazole*. (I) and (II) after Rousseau and Lindwall, *loc. cit.* (III) and (IV) in MeOH.

soluble isomer gave shades with diazo-components corresponding to those from 4-(2-hydroxy-3-naphthoylamino)indazole whereas that from the insoluble isomer gave shades corresponding to those from 6-(2-hydroxy-3-naphthoylamino)indazole.



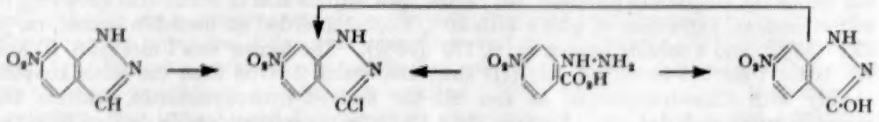
Methylation of 6-nitroindazole to about equal parts of 6-nitro-2- and 6-nitro-1-methylindazole was accomplished by the method of Barclay, Campbell, and Dodds (*J.*, 1941, 113). 7-Nitroindazole in water with methyl sulphate gave 82% of a mixture of isomers, m. p. 98° (53%) and 143° (47%) respectively. The two isomers were reduced and the amines converted into the corresponding hydroxyindazoles the ultraviolet absorption of which (see Figure) showed the hydroxyindazole derived from the isomer of m. p. 98° to correspond to the published curve for 1-methylindazole (Rousseau and Lindwall, *J. Amer. Chem. Soc.*, 1950, **72**, 3047) whereas that for the other hydroxy-indazole corresponded to that for 2-methylindazole.

Benzoylation of the various nitroindazoles likewise gave mixtures of two separable isomers. By analogy the less soluble were considered to be the 2-benzoyl isomers, which

received support from the finding that they were the more stable. The benzoylnitroindazoles were much less stable than the methylnitroindazoles (cf. earlier work on acetyl derivatives: Noelting, *Ber.*, 1904, **37**, 2556).

Ring-closure of diazotised 2-ethyl-5-nitroaniline to 3-methyl-6-nitroindazole was directly comparable with the ring-closure of diazotised 5-nitro-*o*-toluidine. The product was very similar to 6-nitroindazole.

It is stated in B.P. 518,987 without details or proof of orientation that 6-amino-3-chloroindazole (m. p. 185°) is obtained by the chlorination of 6-nitroindazole and reduction of the product. Chlorination of 6-nitroindazole in water at 90—95° afforded 98% of a chloroderivative, m. p. 154°, which gave an amine, m. p. 184°. The nitro-compound was not identical with 5-chloro-6-nitro- (m. p. 172°) or 4-chloro-6-nitro-indazole (m. p. 190°) and the shades obtained with azo-dyes prepared from the amine were similar to those from 6-aminoindazole and dissimilar from those from 4-, 5-, or 7-aminoindazole. Final evidence that the chlorine atom occupied the 3-position was obtained by the action of phosphorus oxychloride or phosphorus pentachloride on 2-hydrazino-4-nitrobenzoic acid or phosphorus trichloride on 6-nitroindazolone which gave the same chloronitroindazole.



Attempts to hydrolyse 3-chloro-6-nitroindazole to 3-hydroxy-6-nitroindazole failed. 2-Hydrazino-4-nitrobenzoic acid (cf. Pfannstiel and Janecke, *Ber.*, 1942, **75** 1096) was cyclised by dehydration in nitrobenzene.

2-*p*-Methoxyphenyl-6-nitroindazole was prepared by Chardonneus and Buch's route (*Helv. Chim. Acta*, 1943, **65**, 874) except that the 2-methylazobenzene was oxidised in 75% yield with hydrogen peroxide in presence of ferrous sulphate instead of nitrosobenzene, the latter giving only small yields.

Reduction of the various nitroindazoles and characterisation of the amines proceeded normally. Conversion into the hydroxyindazoles was readily accomplished by hydrolysis with 10% sulphuric acid at 170—180° (as described in B.P. 697,977), after several other methods for their preparation had failed. Alkali fusion of indazole-5-sulphonic acid, prepared by diazotisation and cyclisation of 3-methylsulphanilic acid, gave only a small amount of *m*-cresol and much alkali-insoluble material. A Bücherer reaction on 5-aminoindazole gave only negligible yields of 5-hydroxyindazole. All the monohydroxyindazoles except 6-hydroxy-7-methylindazole gave nitroso-derivatives which yielded intensely coloured iron complexes.

Fries, Fabel, and Echardt (*Annalen*, 1942, **550**, 31) found that nitration of 6-nitroindazole gave 5 : 6-dinitroindazole which could be reduced to the 5 : 6-diamine and then hydrolysed to 5 : 6-dihydroxyindazole. As evidence for this *ortho*-nitration, the authors stated that the diamine gave the usual *ortho*-condensation products, was not identical with 6 : 7-diaminoindazole, and formed a triazole with nitrous acid. This work has been confirmed. The 5 : 6-diaminoindazole was obtained as remarkably stable white crystals. It reacted with only one equivalent of nitrous acid, presumably giving a triazole since the product did not couple. With phenanthraquinone it gave a yellow product (m. p. 325°) which in concentrated sulphuric acid gave the carmine colour associated with such condensation products. The diamine gave intensely coloured bisazo-dyes and was hydrolysed to the dihydroxyindazole in 85% yield by 20% sulphuric acid at 150°.

Fries *et al.* (*loc. cit.*) state that the ultraviolet absorption spectra of 1-methylindazole and indazole correspond and are different from that of 2-methylindazole. 1-Methyl-6-nitroindazole paralleled 6-nitroindazole in giving exclusively 5-nitration. 2-Methyl-6-nitroindazole, on nitration and reduction, gave mainly an *o*-diamine, but also a *m*-diamine which, however, was not obtained pure. 5-Nitroindazole gave a dinitro-compound (not 5 : 6-dinitroindazole) and thence a *m*-diamine.

Sulphonation of 6-nitroindazole with 20% oleum at 120—130°, followed by reduction,

gave the presumed 6-aminoindazole-5 sulphonic acid obtained from 6-aminoindazole (see below). Identity was established by (*a*) hydrolysis with 10% sulphuric acid to 6-hydroxyindazole (total desulphonation) and (*b*) hydrolysis with water to 6-hydroxyindazole-5-sulphonic acid (see below). Similarly, it was proved that 5-nitroindazole undergoes *meta*-sulphonation, to give 5-nitroindazole-7-sulphonic acid.

The activity of the 5-position in 6-nitroindazole may be explicable in terms similar to those used by Efros (*J. Gen. Chem., U.S.S.R.*, U.S. translation, 1952, **22**, 1063) for 5(6)nitrobenziminazoles which also undergo *ortho*-nitration. On this basis, the link between the 5- and the 6-carbon atom of the indazole nucleus is considered to be preponderantly of single-

bond character; the approximate proportion of 2 : 1 in the ratio of 2-methyl derivatives to 1-methyl derivatives suggests a preponderance of structure (*B*). The only other exception to the naphthalene character of indazole derivatives encountered in this work was the chlorination of 6-nitroindazole in the 3-position which may perhaps have analogy in the side-chain chlorination of the benzene series. Apart from such exceptions, which may be explicable by the directing influence of the heterocyclic nitrogen atoms, the naphthalene character of the indazole ring was generally supported. The resemblance of 5- and 6-hydroxyindazole to β-naphthol was exemplified by their carboxylation to 5-hydroxyindazole-6- and 6-hydroxyindazole-5-carboxylic acid respectively. These acids resembled 2 : 3-hydroxynaphthoic acid and coupled with diazonium compounds without loss of carbon dioxide. The shades of azo-dyes prepared from the various indazole derivatives were similar to those from the naphthalene analogues. The much stronger bathochromic effect of a hydroxy- or an amino-group in the 5- and the 7-position compared with the 4- and the 6-position was evident throughout the series.

Little has previously been recorded on indazolesulphonic acids. After our work on them was completed, Peticolas and Sureau (*Bull. Soc. chim. France*, 1950, 466) described the preparation of indazole-4-, -5-, -6-, and -7-sulphonic acid by diverse routes and characterised them as benzoylguanidinium salts and sulphonyl chlorides, and by alkali fusion to the hydroxyindazoles, the last being the main criterion for configuration. Our results differed in some respects; possibly the sulphonation conditions are critical (cf. naphthalene). It is surprising that the indazole nucleus is stable to caustic fusion. The main divergencies lie in the sulphonation products of 5- and 6-aminoindazole. Peticolas and Sureau concluded that oleum afforded 6-aminoindazole-7- and 5-aminoindazole-4-sulphonic acid. We, however, obtained acids which coupled readily, both before and after acid hydrolysis, to give soluble azo-dyes, and consider sulphonation to have given 6-aminoindazole-4- and 5-aminoindazole-7-sulphonic acid. In view of these apparent anomalies the configurations below are only tentative; they are based on three criteria, namely, coupling reactions of the products, configuration of the starting material, and the melting point of the *S*-*p*-chlorobenzylthiuronium hydroxyindazolesulphonates. It is pertinent that the compounds considered to be 6-hydroxyindazole-7- and 5-hydroxyindazole-4-sulphonic acid did not couple.

Sulphonation of 6-aminoindazole with 20% oleum at 120° gave a product which with diazotised *p*-chloroaniline in alkali readily gave a soluble red azo-dye. Coupling was assumed to take place in the 7-position and the constitution tentatively considered to be 6-aminoindazole-4-sulphonic acid. Heating this product at 180° with a molar equivalent of 10% sulphuric acid gave a hydroxyindazolesulphonic acid without detectable desulphonation. This compound gave a soluble orange azo-dye.

Heating 6-aminoindazole sulphate with sulphuric acid in *o*-dichlorobenzene at 176° gave a different sulphonic acid. This also coupled readily with diazotised *p*-chloroaniline to give a soluble red azo-dye, indicating the 7-position to be unoccupied, and so was considered to be 6-aminoindazole-5-sulphonic acid which, as stated above, was also obtained from 6-nitroindazole by sulphonation and reduction. Heating this new acid at

180° with a molar equivalent of 10% sulphuric acid gave a quantitative yield of 6-hydroxyindazole. Desulphonation preponderated even with only traces of mineral acid or with neutral solutions in the presence of iron. Heating at 180° with water alone in glass, however, gave good yields of, presumably, 6-hydroxyindazole-5-sulphonic acid. This also coupled readily, to give a soluble orange azo-dye, and its *S*-*p*-chlorobenzylthiuronium salt differed from that of its isomer.

With 100% sulphuric acid at 100° 6-hydroxyindazole gave a monosulphonic acid which did not couple; its *S*-*p*-chlorobenzylthiuronium salt differed from that of the preceding acid. The product is considered to be 6-hydroxyindazole-7-sulphonic acid. Prolonged heating of this sulphonic acid or 6-hydroxyindazole with 95% sulphuric acid at 130° gave a mixture containing 20—30% of 6-hydroxyindazole-5-sulphonic acid. Treatment with ammonia in the presence of sodium hydrogen sulphite gave 6-aminoindazole-7-sulphonic acid which did not couple in acetic acid.

Nitrosation of 6-hydroxyindazole, followed by reaction with sodium hydrogen sulphite, as in the preparation of 4-amino-3-hydroxynaphthalene-1-sulphonic acid, gave a product considered to be 7-amino-6-hydroxyindazole-4-sulphonic acid. The product diazotised in the presence of copper sulphate to give a stable diazo-compound which coupled with α- or β-naphthol in 2-ethoxyethanol.

Application of the same series of reactions to 5-aminoindazole and 5-hydroxyindazole gave analogous products except that 5-aminoindazole-6-sulphonic acid was desulphonated even with water in glass, so that 5-hydroxyindazole-6-sulphonic acid was not prepared.

4-Methyl-5-nitrometanilic acid and nitrous acid gave 4-nitroindazole-6-sulphonic acid and thence the amino- and hydroxy-acid, the last giving a soluble orange azo-dye.

Experimental

Coupling was with diazotised *o*-chloroaniline unless otherwise stated.

Preparation of Nitroindazoles.—The method of *Org. Synth.*, **20**, 72, for the preparation of 5-nitroindazole was applied to a series of *o*-toluidines, the product being isolated by distillation of the glacial acetic acid under reduced pressure and recrystallised from 10% acetic acid or ethanol. Thus were obtained: 4- (79%), m. p. 202°, 5- (72%), m. p. 180°, 6- (88·5%), m. p. 209°, and 7-nitroindazole (71%), m. p. 180° (Noelting, *loc. cit.*, gives m. p. 203°, 181°, 208°, and 186·5—187·5°, respectively); 5-methyl-6-nitroindazole (53%), m. p. 173° (Noelting, *loc. cit.*, gives m. p. 173—174°); *4-chloro-* (81%), pale yellow needles (from water), m. p. 190° (Found: C, 42·0; H, 1·9; N, 20·9; Cl, 18·1. $C_7H_4O_2N_2Cl$ requires C, 42·5; H, 2·0; N, 21·25; Cl, 17·95%), and *5-chloro-6-nitroindazole* (34%), yellow needles (from water), m. p. 172° (Found: C, 42·1; H, 2·1; N, 21·3; Cl, 17·8%); *6-methoxy-5-nitroindazole* (35%), fawn, m. p. 191° (Found: C, 49·3; H, 3·45; N, 21·2. $C_8H_7O_3N_3$ requires C, 49·7; H, 3·6; N, 21·75%); *6-chloro-5-nitroindazole* (63·3%), pale brown, m. p. 213° (Found: N, 20·8; Cl, 18·2%); *6-methyl-4-nitroindazole* (73·5%), buff, m. p. 204° yield (Found: N, 23·2. $C_8H_7O_2N_3$ requires N, 23·7%); *3-methyl-6-nitroindazole* (73·5%), cream-coloured, m. p. 182° (Found: C, 54; H, 4·1; N, 23·4. $C_8H_7O_2N_3$ requires C, 54·2; H, 3·95; N, 23·7%).

Ring-closure of 3-Nitro-2 : 6-xylidine.—The mixture (110 g.) of isomers produced, m. p. 209—210°, was extracted three times with boiling 50% v/v ethyl alcohol (1 l.) for ½ hr. The insoluble 7-methyl-6-nitroindazole (see below), dried at 100°, was fawn-coloured (64 g.) and had m. p. 222° (Noelting, *loc. cit.*, gives m. p. 222·5°). The ethanol liquors were evaporated to 500 c.c. and allowed to crystallise. 7-Methyl-4-nitroindazole (see below) was filtered off and dried (37 g.; m. p. 179°; Noelting, *loc. cit.*, gives m. p. 175—176°).

Methylation of 7-Nitroindazole.—To 7-nitroindazole (60 g.), dissolved in water (1·4 l.) and 32% sodium hydroxide solution (200 c.c.) at 80°, methyl sulphate (132 g.) was added while the temperature was allowed to fall to 65° during ½ hr. The mixture was stirred at 60—65° for 2 hr. After cooling to 30° the fawn precipitate was filtered off and recrystallised from butanol repeatedly to separate *2-methyl-7-nitroindazole* (30·6 g.), m. p. 143° (Found: N, 23·8. $C_8H_7O_2N_3$ requires N, 23·7%), from *1-methyl-7-nitroindazole* (34·6 g.), m. p. 98° (Found: N, 23·4%).

Methylation of 6-Nitroindazole.—Methylation of 6-nitroindazole by the same method followed by separation by Barclay, Campbell, and Dodds's method (*J.*, 1941, 113; fractionation from methyl alcohol) gave 1-methyl-, m. p. 122°, and 2-methyl-6-nitroindazole, m. p. 158° (Barclay *et al.* give m. p. 125° and 160° respectively).

Benzoylation of Nitroindazoles.—Benzoylation of 6-nitroindazole in dilute sodium hydroxide

solution at 50° gave a mixture, m. p. 138° (62% yield). Repeated recrystallisation from methanol separated the *2-benzoyl isomer*, m. p. 165° (20%) (Found : N, 15·2. $C_{14}H_9O_3N_3$ requires N, 15·7%), from the more soluble *1-benzoyl isomer*, m. p. 161° (42%) (Found : N, 14·9%).

5-Methyl-6-nitroindazole similarly afforded a mixture (73·5%; m. p. 122°) of the *1-benzoyl compound*, m. p. 163° (37·5%) (Found : N, 14·7. $C_{15}H_{11}O_3N_3$ requires N, 14·9%), and the *2-benzoyl isomer* (36%), m. p. 162° (Found : N, 15·2%), separated by crystallisation from butanol.

5-Nitroindazole afforded a mixture, m. p. 172° (77%), separated by methanol into 1- (50·5%), m. p. 190° (Found : N, 15·4%), and *2-benzoyl-5-nitroindazole* (Found : N, 15·8%). Similar benzoylation of 6-chloro-5-nitroindazole and crystallisation from butanol gave 1- (24%), m. p. 203° (Found : N, 13·3. $C_{14}H_8O_3N_3Cl$ requires N, 13·9%), and *2-benzoyl-6-chloro-5-nitroindazole* (46·5%), m. p. 192° (Found : N, 13·5%). Benzoylation of 6-methoxy-5-nitroindazole and crystallisation from methanol gave 1- (20%), m. p. 192° (Found : N, 13·8. $C_{15}H_{11}O_4N_3$ requires N, 14·1%), and *2-benzoyl-6-methoxy-5-nitroindazole* (40%), m. p. 186° (Found : N, 14·3%).

Chlorination of 6-Nitroindazole.—B.P. 518,987 states without experimental details that 3-chloro-6-nitroindazole is obtained by chlorination of 6-nitroindazole. Chlorine was passed for 3 hr. into a suspension of 6-nitro-indazole (0·1 mole) in water (100 c.c.) at 95° ± 2°. The precipitate, recrystallised from ethanol, gave yellow needles (18 g.), m. p. 154° (*3-chloro-6-nitroindazole*) (Found : Cl, 18·2. $C_7H_4O_2N_3Cl$ requires Cl, 17·95%). The mixed m. p. with 5-chloro-6-nitroindazole (m. p. 185°) was 111—113° and with 4-chloro-6-nitroindazole (m. p. 184°) was 136°. Attempts to convert it into 3-amino-6-nitroindazole failed.

6-Nitroindazolone (*3-Hydroxy-6-nitroindazole*) (cf. Pfannstiel and Janecke, *Ber.*, 1942, **75**, 1096).—4-Nitroanthranilic acid (113 g.; m. p. 271°) was dissolved in water (1·7 l.) and 32% sodium hydroxide solution (60 c.c.). 40% Sodium nitrite solution was added (120 c.c.) and the resulting dark orange solution added during 20 min. to 36% hydrochloric acid (214 c.c.) and the minimum amount of ice to hold the temperature below 5°. The resulting solution was added at 0—5° to a mixture of 32% sodium hydroxide solution (260 c.c.) and 40% sodium hydrogen sulphite solution (427 c.c.), and stirring at 0—10° continued for 1 hr. 36% Hydrochloric acid (820 c.c.) was added and the temperature raised to 60° during ½ hr. After being stirred at room temperature overnight, sodium chloride was added to 20% concentration, the mixture cooled to 10°, and the hydrazine hydrochloride filtered off. The hydrazine hydrochloride paste (220 g., 60% yield) was added portionwise during 2 hr. to nitrobenzene (350 g.) during gradual distillation to remove water, the volume being held constant by addition of nitrobenzene. Then distillation was continued for a further ½ hr. The mixture was cooled in ice, diluted with benzene (200 c.c.), and filtered. The filter cake was suspended in water (500 c.c.) and steam distilled to remove benzene and nitrobenzene. The solution was treated with carbon and filtered, and the filtrate cooled. The orange-red needles of 3-hydroxy-6-nitroindazole were filtered off and dried at 60° (60 g.; m. p. 237·5°). A single recrystallisation from water raised the m. p. to 243° (Pfannstiel and Janecke, *loc. cit.*, give m. p. 244°) (Found : N, 23·2. Calc. for $C_7H_5O_3N_3$: N, 23·45%). No success attended attempts to aminate 3-hydroxy-6-nitroindazole.

Conversion of 3-Hydroxy-6-nitroindazole into 3-Chloro-6-nitroindazole.—Various methods for the ring-closure of 2-hydrazinobenzoic acid gave unsatisfactory results with 2-hydrazino-4-nitrobenzoic acid; use of phosphorus trichloride or phosphorus oxychloride giving 3-chloro-6-nitroindazole. 3-Hydroxy-6-nitroindazole was converted into 3-chloro-6-nitroindazole by an excess of boiling phosphorus trichloride : the product, recrystallised from ethanol, had m. p. and mixed m. p. 154°.

2-p-Methoxyphenyl-6-nitroindazole (cf. Chardonneus and Buch, *loc. cit.*).—The preparation of *4'*-methoxy-2-methyl-3-nitroazobenzene offered no difficulty but ring-closure by nitrosobenzene gave only a negligible yield of material of the correct m. p. A suspension (80 g.) in glacial acetic acid (450 c.c.) was heated with hydrogen peroxide (100-vol.; 49 c.c.) in the presence of ferrous sulphate (3 g.) at 80—85°; the product (75%), purified by extraction with ethanol, had m. p. 150° (Chardonneus and Buch give m. p. 152°).

Preparation of Aminoindazoles.—Since reduction of nitroindazoles with iron in water (method A) sometimes caused decomposition, it was often accomplished in alcohol (method B) or by hydrogenation in presence of Raney nickel (method C) (cf. Kwurther and Lucas, *J. Amer. Chem. Soc.*, 1943, **65**, 1804). *Products* (see Table) were recrystallised from alcohol or water, and converted into the 3-hydroxy-2-naphthoyl derivatives (cf. B.P. 707,897), which were coupled with diazotised *o*-chloroaniline.

Preparation of the Hydroxyindazoles.—Aminoindazoles gave the corresponding hydroxyindazoles readily on acid hydrolysis (cf. B.P. 697,977). This method was also applicable to

the preparation of several hydroxyindazolesulphonic acids. Alternative methods gave very poor results, negligible amounts being formed by caustic fusion of the sulphonic acid and diazotisation of the amino-compound followed by boiling with sulphuric acid afforded low yields of impure products.

Aminoindazoles.

Substituent at position							Method of prep.	Yield (%)	M. p.	Found N (%)	Reqd. N (%)	2 : 3-HO·$C_{10}H_7$·CO deriv. M. p.	2 : 3-HO·$C_{10}H_7$·CO deriv. coupling, shade of orange
1	2	3	4	5	6	7							
			NH_2				C	92·5	150° [a]	31·3		296°	Yellow
				NH_2			C	82	183° [b]	31·25	31·6	245	Red
					NH_2		A	86	209° [c]	31·4		274	
						NH_2	C	86	162	31·6		218	Red
			Me		NH_2		B	71·5	165	28·3	28·6	258	
			Cl		NH_2		C	88	194	25·2 [d]	25·05	248	Dull
			Cl		NH_2		C	88	198	24·8 [e]	25·05	294	
			NH_2	Cl			A	88	178	—[f]		252	Red
			NH_2	OMe			B	90	165	25·3	25·75	263	Red
					NH_2	Me	C	84	182	28·5		299	
			NH_2			Me	C	87·5	124	28·2		279	Yellow
			NH_2		Me		C	79	126	28·2		279	Yellow
		Me			NH_2		C	91	205	28·2	28·6	284	
	Me				NH_2		B	81	165	28·4		212	Dull
Me					NH_2		C	75·3	130	28·3		180	Dull
Me						NH_2	B	72	135	28·4		—	
	Me					NH_2	B	(90) [g]	73	28·2		—	
Bz					NH_2		C	80	194	17·2	17·7	257	
	Bz				NH_2		C	70	179	17·4	17·7	266	
	Bz			Me	NH_2		C	74	185	16·3	16·7	249	Dull
Bz				NH_2			—[h]	90	178	16·9	17·7	249	Red
	Bz			NH_2			—[h]	60	170	17·5	17·7	276	Red
		Cl			NH_2		C	76	184	25·2 [i]	25·05	269	
	Ar [j]				NH_2		—	32	174	17·1	17·6	211	Dull
		OH			NH_2		C	80·5	285	28·2	28·2	—	

[a] Plates. [b] Prisms. [c] Needles. [d] Found: Cl, 20·8. Reqd.: Cl, 21·2%. [e] Found: Cl, 20·6%. [f] Found: Cl, 21·0%. [g] Partly oily. [h] Prep. by Zn in EtOH. [i] Found: Cl, 20·6. Reqd.: Cl, 21·2%. [j] Ar = *p*-MeO·C_6H_4; prep. by aq. Na_2S.

6-Hydroxyindazole. 6-Aminoindazole (66·5 g.), 96% sulphuric acid (50 g.), and water (500 c.c.) were heated in an enamel-lined autoclave (750-c.c. capacity) to 170° in 1 hr. and then at 170—175° for 10 hr. (pressure 200—220 lb. per sq. in.). The pale brown solution was filtered, neutralised to Congo-red with sodium hydroxide solution, and cooled to 30°. The 6-hydroxyindazole was filtered off, washed with water, and dried at 60° (65 g., 95·5%; m. p. 216°). Recrystallisation from water gave pale fawn crystals, m. p. 217° (Found: N, 19·7. Calc. for $C_7H_6ON_2,\frac{1}{2}H_2O$: N, 19·6%). 6-Hydroxyindazole gave an orange colour on coupling and a red-brown colour with ferric chloride.

5-Hydroxyindazole. 5-Aminoindazole (66·5 g.), 100% sulphuric acid (50 g.), and water (500 c.c.) were heated at 175—180° as above (150 lb. per sq. in.). The mixture was made alkaline to Clayton Yellow by addition of 32% sodium hydroxide solution, acidified to Clayton Yellow with acetic acid, filtered, acidified to Brilliant Yellow with acetic acid, and treated with salt to 20% concentration. After 3 hr. the white crystals were filtered off and dried (62·5 g., 93%; m. p. 181—183°). Recrystallised from water, the product had m. p. 186° (Found: N, 18·7. Calc. for $C_7H_6ON_2,H_2O$: N, 18·4%). On coupling it gave a reddish-orange colour, and with ferric chloride a brown one.

4-Hydroxyindazole. The procedure described for 6-hydroxyindazole gave 4-hydroxyindazole in 72% yield, as needles, m. p. 163° (Found: N, 21·2. Calc. for $C_7H_6ON_2$: N, 20·9%); with ferric chloride it gave a yellow-brown, and on coupling a yellowish-orange colour.

7-Hydroxyindazole. The procedure described for 5-hydroxyindazole gave 64% of 7-hydroxyindazole, as pale pink needles (from water), m. p. 174° (Found: N, 21·0%), giving a brown precipitate with ferric chloride and a yellow-brown colour on coupling.

7-Hydroxy-1-methylindazole. The procedure described for 6-hydroxyindazole gave 79% of this *compound* as pale grey needles (from water), m. p. 163° (Found: N, 18·8. $C_8H_8ON_2$ requires N, 18·9%) (see Figure).

7-Hydroxy-2-methylindazole. Similarly, *7-hydroxy-2-methylindazole* (71%) was obtained as pale pink needles, m. p. 179°, from water (Found: N, 19·3%) (see Figure).

4-Hydroxy-6-methylindazole (64·2%), pale orange needles, m. p. 176° (Found : N, 19·2%) (orange colour on coupling; pale brown with ferric chloride), and *4-hydroxy-7-methylindazole* (68%), yellow needles, m. p. 179° (Found : N, 19·1%) (orange colour on coupling; red-brown with ferric chloride), *6-hydroxy-7-methylindazole* (62%), cream needles, m. p. 164° (Found : N, 18·5%) (does not couple; brown colour with ferric chloride), and *6-hydroxy-3-methylindazole* (57·5%), m. p. 221° (Found : N, 19·2%) (bright orange on coupling; a red colour with ferric chloride), were similarly prepared.

Carboxylation of 5- and 6-Hydroxyindazole.—6-Hydroxyindazole-5-carboxylic acid. A solution of 6-hydroxyindazole (75 g.) in water (500 c.c.), with 50% w/v potassium hydroxide (60 c.c.) to alkalinity to Clayton Yellow, was evaporated to dryness under reduced pressure. The resulting powder was passed through a 60-mesh sieve, and heated in a rotating autoclave at 130°/20 mm. for ½ hr. The autoclave was charged with carbon dioxide to 200 lb. and heated to 210° during 3 hr. Heating at 210° ± 2° and 300 lb./sq. in. was continued for 12 hr. The mixture was dissolved in boiling water (300 c.c.), neutralised to faint alkalinity to Brilliant Yellow with 36% hydrochloric acid, cooled to 10°, and filtered. The filtrate was acidified to Congo-red with 36% hydrochloric acid. The white precipitate was filtered off, washed free from mineral acid with water, and dried at 60° (70 g.). Recrystallisation from butanol gave the *acid* as cream prisms, m. p. 202° (decomp.) (Found : N, 15·6. $C_8H_6O_3N_2$ requires N, 15·7%). The product dissolved in dilute sodium carbonate solution, coupled readily to give an orange colour, and gave a reddish-brown colour with ferric chloride.

5-Hydroxyindazole-6-carboxylic acid. 5-Hydroxyindazole (27 g.) was ground with potassium hydrogen carbonate (50 g.), the mixture passed through a 60-mesh sieve, and heated in a rotating autoclave at 210°/20 mm. during 1½ hr. Carbon dioxide was then passed in, to 420 lb./sq. in. Heating at 210° ± 2° was continued for 15 hr. during which the pressure dropped to 365 lb./sq. in. The autoclave was cooled and the solid product dissolved in water (500 c.c.) at 60°. The solution was filtered from insoluble material (7 g.), and the filtrate acidified to Congo-red with 36% hydrochloric acid. The white precipitate was filtered off, washed with water, and dried (24 g.). The *acid* crystallised from butanol as white needles, m. p. 205° (Found : N, 15·5%). The product was readily soluble in dilute sodium carbonate solution, coupled readily to give a reddish-orange solution, and gave a bluish-brown colour with ferric chloride.

Products from the Nitration and Sulphonation of Nitroindazoles.—Nitration of 6-nitroindazole (cf. Fries *et al.*, *loc. cit.*). To a solution of 6-nitroindazole (250 g.) in 96% sulphuric acid (2·5 l.) mixed 96% sulphuric (500 c.c.) and 96% nitric acid (500 c.c.) were added at 8—10° during 1 hr. Stirring at 8—10° was continued for 3 hr. and the solution poured on ice (8 kg.). The canary-yellow suspension was filtered, and the 5 : 6-dinitroindazole was washed, dried at 100° (290 g., 91%), and recrystallised from 10% acetic acid as yellow needles, m. p. 225° (Fries *et al.*, *loc. cit.*, give m. p. 224°, 70% yield).

5 : 6-Diaminoindazole. 5 : 6-Dinitroindazole (290 g.) was added during ¾ hr. to a solution of stannous chloride (2·9 kg.) in 36% hydrochloric acid (2·9 l.) with stirring at 5°. The first portion added (100 g.) raised the temperature to 50° and thereafter the temperature was held at 50—52° by cooling. The suspension of the double *salt* was stirred at 50—52° for 3 hr., cooled to 5°, and filtered off. A sample was recrystallised from water (Found : N, 13·6; Cl, 34·25. $C_7H_{10}N_4,2HCl,SnCl_2$ requires N, 13·6; Cl, 34·3%). The double salt paste was dissolved in water (3 l.) at 90°, carbon (10 g.) added, and, after 10 minutes' stirring at 90°, the solution was filtered and poured into water (1·3 l.) and 32% sodium hydroxide solution (1·3 l.) with stirring. The resulting white suspension was boiled for 10 min., cooled to 35°, and filtered. The solid was again boiled with dilute sodium hydroxide solution (2 l.), cooled to 35°, filtered, and washed free from alkali with water. The precipitated diamine was dried at 60° (85%; m. p. 280·5°) and recrystallised from water as white needles, m. p. 286° (Found : C, 56·6; H, 5·2; N, 37·2. Calc. for $C_7H_8N_4$: C, 56·7; H, 5·4; N, 37·8%). The product did not deteriorate in colour or nitrite strength in 4 years. It coupled readily with two equivalents of a diazo-compound to give deeply coloured products and absorbed only on equivalent of nitrous acid to give a triazole. Condensation in alcohol with a molar proportion of phenanthraquinone gave an orange derivative, m. p. 325° (decomp.), which dissolved in concentrated sulphuric acid to a carmine solution.

5 : 6-Dihydroxyindazole. The conditions given by Fries *et al.* (*loc. cit.*) gave a product difficult to purify. The following gave the best results : 5 : 6-Diaminoindazole (41·3 g.) and 20% w/w sulphuric acid (560 c.c.) were heated in an enamel-lined autoclave for 5 hr. at 145—150°, then cooled to 10° for ½ hr. and the 5 : 6-dihydroxyindazole sulphate was filtered off. The solid was stirred at 98—100° with water (500 c.c.) and sodium acetate crystals (43 g.) for 5 min.,

the solution filtered hot, and the residue extracted twice with hot water (200, 150 c.c.). The combined filtrates were boiled with carbon (5 g.) for 5 min., then filtered, and the filtrate acidified to Congo-red (faint purple) with 36% hydrochloric acid. The resulting white suspension was cooled in ice for 2 hr., then filtered and the product washed with water (100 c.c.), dried at 60°, (35·7 g.; m. p. 232·5°) and recrystallised from water (m. p. 234°; Fries *et al.*, *loc. cit.*, give m. p. 235°) (Found: N, 18·6. Calc. for $C_7H_6O_2N_2$: N, 18·7%).

Nitration of 1-*methyl*-6-*nitroindazole*. This indazole was nitrated as described for 6-nitroindazole. The product (m. p. of sample recrystallised from 10% acetic acid, 171°) was reduced similarly to a ***diamine*** which crystallised from water as white prisms, m. p. 263° (Found: C, 59·4; H, 6·7; N, 34·5. $C_8H_{10}N_4$ requires C, 59·2; H, 6·2; N, 34·55%). This absorbed one equiv. of nitrous acid and gave a phenanthraquinone derivative, m. p. 291° (carmine in sulphuric acid).

Nitration of 2-*methyl*-6-*nitroindazole*. Similar nitration of 2-methyl-6-nitroindazole gave a *product*, m. p. 213° (Found: N, 24·4. $C_8H_8O_4N_4$ requires N, 25·2%), reduced to a product which behaved as a *m*-diamine in that it gave a brown precipitate with nitrous acid and was very susceptible to air-oxidation. When purified by recrystallisation from water, 5 : 6-*diamino*-2-*methylindazole* crystallised in white needles, m. p. 226° (Found: C, 59·6; H, 7·1; N, 34·8%). The phenanthraquinone derivative, m. p. 291°, gave a mixed m. p. of 256° with the 1-methyl isomer and in concentrated sulphuric acid gave a red solution. Attempts to characterise the compound remaining in the liquors gave intractable tars. Catalytic hydrogenation of the dinitro-compound gave a larger amount of this impurity.

Nitration of 5-*nitroindazole*. 5-Nitroindazole (20 g.) in 98% sulphuric acid (200 g.) at 10° was treated with 95% nitric acid (40 c.c.) and 98% sulphuric acid (40 c.c.) dropwise during 3 hr. at 8—12°, and stirring at 8—12° continued for 3½ hr. The mixture was poured on ice (750 g.), then filtered, and the residue washed with water (400 c.c.) and with dilute ammonia solution (500 c.c.), dried at 70° (19 g.), and recrystallised from butanol as yellow prismatic needles, m. p. 222·5° (Zincke, *Annalen*, 1905, **339**, 224, gives m. p. 215° for 5 : 7-dinitroindazole prepared from 4 : 6-dinitro-*o*-toluidine). Reduction of the dinitro-derivative with stannous chloride was unsatisfactory owing to the high solubility and instability of the diamine. It was satisfactory as follows: the dinitro-compound (5 g.) in ethanol (90 c.c.) was hydrogenated at 20—25°/400 lb. per sq. in. in the presence of 50% Raney nickel (5 g.). Filtration and evaporation to dryness in nitrogen gave a pale fawn product (2·5 g.) which darkened rapidly in air and gave no condensation products typical of *o*-diamines. Attempted hydrolysis by the method used for 5 : 6-diaminoindazole resulted in de-amination, a 23% yield of 5-hydroxyindazole (m. p. and mixed m. p. 183°) being isolated by recrystallisation of the heterogeneous product from water.

Sulphonation of 6-*nitroindazole*. 6-Nitroindazole (49 g.) was added below 50° to 20% oleum (200 g.). The mixture was heated to 120° in ½ hr. and stirred at 120—130° for 5 hr., then poured on ice (100 g.) and water (100 c.c.), the resulting solution was diluted to 1 l. with water, and the sulphate was removed by addition of calcium oxide at 95°. The precipitate was extracted with hot water and the combined filtrates treated with sodium carbonate (16 g.). After filtration from calcium carbonate the liquid (5 l.) was evaporated to dryness. The product (59 g.) was dissolved in water (300 c.c.) and added during 3 hr. to iron filings (100 g.), ferrous sulphate (10 g.), and water (300 c.c.) with stirring at 90—95°. After a further hour's stirring at 95°, soluble iron was removed by the addition of 15% sodium carbonate solution (10 c.c.), the iron residue was filtered off and extracted with hot water, and the combined filtrates (2 l.) were acidified with hydrochloric acid and evaporated to dryness (50 g.). The crude product was purified as described below, yielding 6-*aminoindazole*-5-*sulphonic acid* (Found: N, 18·7. $C_7H_7O_3NS,\frac{1}{2}H_2O$ requires N, 18·9%). Hydrolysis with water as described for 6-hydroxyindazole-5-sulphonic acid (see below) gave a product, the *S*-*p*-chlorobenzylthiuronium salt of which had m. p. and mixed m. p. 226° with that from 6-hydroxyindazole-5-sulphonic acid.

Sulphonation of 5-*nitroindazole*. Sulphonation of 5-nitroindazole (49 g.) and reduction of the product as described above for 6-nitroindazole gave an *aminoindazolesulphonic acid* (36 g.), which was purified by reprecipitation from alkaline solution with sulphuric acid (Found: N, 19·5. $C_7H_7O_3N_2S$ requires N, 19·7%). Hydrolysis with dilute sulphuric acid as described below for 5-aminoindazole-7-sulphonic acid gave 5-hydroxyindazole-7-sulphonic acid (*S*-*p*-chlorobenzylthiuronium salt, m. p. 204°).

6-*Aminoindazole*-4-*sulphonic acid*. 6-Aminoindazole (53·2 g.) was added during ½ hr. to 20% oleum (200 g.) with stirring at <50°. After further stirring for 1 hr. the mixture was heated and stirred at 120—125° for 2 hr. The mixture was poured on ice (100 g.) and water

(200 c.c.), and treated with calcium oxide at 95°; the precipitate was converted into the sodium salt and its solution evaporated to dryness (78 g.). Purified by solution in dilute sodium carbonate (carbon), acidification with sulphuric acid, and crystallisation, the *acid* was colourless (Found: C, 36·4; H, 4·2; N, 18·6; S, 13·8. $C_7H_7O_3N_3S,H_2O$ requires C, 36·4; H, 3·9; N, 18·2; S, 13·8%). It absorbed one equiv. of nitrous acid and coupled in acetic acid solution with one equiv. of diazo-compounds.

6-Hydroxyindazole-4-sulphonic acid. 6-Aminoindazole-4-sulphonic acid (0·4 mole), water (500 c.c.), and 96% sulphuric acid (50 g.) were heated in an enamel-lined autoclave at 175—180° for 10 hr., then treated as above. The crude product (118 g.) was boiled in water (600 c.c.) with carbon (5 g.) and filtered at 100°. The filtrate was acidified to Congo-red (purple), and cooled to 30°. The white crystals, washed with water and dried at 100° (35 g.) (Found: N, 13·7. $C_7H_6O_4N_2S$ requires N, 13·1%), were soluble in water and coupled with one equiv. of *p*-chlorodiazobenzene to a soluble yellowish-orange dye and with ferric chloride gave a brown precipitate. The *S*-*p*-chlorobenzylthiuronium salt had m. p. 212·5—213·5°.

5-Aminoindazole-7-sulphonic acid. 5-Aminoindazole (39·9 g.) was added below 50° to 20% oleum (150 g.) and the mixture stirred at 120—125° for 2 hr. and poured on ice (300 g.). After 1 hr. the precipitated *acid* (63 g.) was purified as was 6-aminoindazole-4-sulphonic acid (Found: C, 39·2; H, 3·4; N, 19·3; S, 15·0. $C_7H_7O_3N_3S$ requires C, 39·4; H, 3·3; N, 19·7; S, 15·0%).

5-Hydroxyindazole-7-sulphonic acid. The foregoing acid (0·15 mole), 96% sulphuric acid (30 g.), and water (300 c.c.) were heated in an enamel-lined autoclave at 175—180° for 12 hr. The solution was boiled with carbon (5 g.) and filtered. The filtrate was neutralised with sodium acetate, treated with sodium chloride to 10% concentration, and cooled in ice for 3 hr. The white precipitate (27 g.) recrystallised from dilute acetic acid (Found: C, 38·8; H, 2·9; N, 13·0; S, 15·1. $C_7H_6O_4N_2S$ requires C, 39·2; H, 2·8; N, 13·1; S, 14·9%). The *acid* coupled with one equiv. of *p*-chlorodiazobenzene to give a reddish-orange and gave a red precipitate with ferric chloride. The *S*-*p*-chlorobenzylthiuronium salts had m. p. 205°.

6-Aminoindazole-5-sulphonic acid (cf. Adams *et al.*, B.I.O.S. report 1153). In a 2-l. 3-necked flask, equipped with ¼" diam. delivery tube approx. 7" long to the top of a 500 c.c. capacity calcium chloride trap, agitator with rubber gland and thermometer. The calcium chloride trap had two arms with taps, one to return to the flask and the other, at a lower level, to draw off. The top of the trap was connected to a vacuum line through a water reflux condenser. This apparatus was designed to ensure easy separation of water and return of *o*-dichlorobenzene to the flask. Heating was applied by an electric oil bath. 6-Aminoindazole sulphate (109 g.), mixed with 100% sulphuric acid (53·5 g.), was heated with *o*-dichlorobenzene (980 c.c.) to 160° with decreasing vacuum during 3 hr. and held at 100° under partial vacuum to maintain reflux through the calcium chloride trap for 1 hr. The temperature was raised to reflux (176°) without vacuum and stirring and refluxing were continued overnight. The *o*-dichlorobenzene was decanted and the residual solid dissolved in water (1 l.) and 32% sodium hydroxide solution (135 g.). The solution was boiled with charcoal (10 g.) and filtered and the filtrate acidified to Congo-red with sulphuric acid and cooled. The *acid* (80 g.) was recrystallised from dilute sulphuric acid (Found: C, 38·4; H, 4·0; N, 18·5; S, 14·5. $C_7H_7O_3N_3S,\frac{1}{2}H_2O$ requires C, 37·8; H, 3·6; N, 18·9; S, 14·4%). It absorbed one equiv. of nitrous acid and, when coupled in dilute acetic acid with diazotised *p*-chloroaniline, gave a soluble azo-derivative.

6-Hydroxyindazole-5-sulphonic acid. 6-Aminoindazole-5-sulphonic acid and dilute sulphuric acid gave 6-hydroxyindazole (desulphonation). The acid (21·3 g.) was heated in a glass-lined autoclave with water (150 c.c.) at 155—160° for 10 hr. The solution was made alkaline to Brilliant Yellow with sodium carbonate solution, cooled to 15°, and filtered from a trace of 6-hydroxyindazole. The filtrate was evaporated to dryness *in vacuo* (24 g.). Recrystallisation from dilute sulphuric acid resulted in desulphonation. The unpurified product was of 82% strength by coupling and gave an orange dye with diazotised *p*-chloroaniline and a blue colour with ferric chloride. The *S*-*p*-chlorobenzylthiuronium salt had m. p. 227·5°.

5-Aminoindazole-6-sulphonic acid. Treatment of 5-aminoindazole sulphate as for 6-aminoindazole-5-sulphonic acid gave *5-aminoindazole-6-sulphonic acid*, pale grey needles from dilute sulphuric acid (Found: C, 39·2; H, 3·4; N, 19; S, 15·0%), which absorbed one equiv. of nitrous acid and with diazotised *p*-chloroaniline in acetic acid gave a red water-soluble azo-dye. Attempts to hydrolyse the presumed 5-aminoindazole-6-sulphonic acid gave only 5-hydroxyindazole.

6-Hydroxyindazole-7-sulphonic acid. 6-Hydroxyindazole (27 g.) was added during ½ hr. to 100% sulphuric acid (100 g.) with stirring at 20—30°. The reaction was slightly exothermic and, when the addition was 70% complete, crystallisation began. The mixture was then stirred at 100° for 1 hr., poured on ice (200 g.) and water (200 c.c.), and kept for 1 hr. The white

precipitate was recrystallised from water (yield 93·3%) (Found : C, 39·2; H, 2·7; N, 13·3; S, 14·85. $C_7H_6O_4N_2S$ requires C, 39·2; H, 2·8; N, 13·1; S, 14·9%). The *product* did not couple but gave a mauve precipitate with ferric chloride. The *S*-*p*-chlorobenzylthiuronium salt had m. p. 204·5°. Heating this product with 95% sulphuric acid (10 parts) to 130° for 5 hr., or 6-hydroxy-indazole (27 g.) with 95% sulphuric acid (100 g.) at 130° for 5 hr., gave a product which had a coupling strength of 32·5—34% and gave an orange soluble dye with diazotised *p*-chloroaniline. Crystallising the *S*-*p*-chlorobenzylthiuronium salt from 60% ethanol gave approx. equal proportions of a fraction, m. p. and mixed m. p. with above derivative 202—204·5° (hydrolysis with dilute sodium hydroxide solution regenerated the same hydroxyindazolesulphonic acid) and a fraction of m. p. 224° and mixed m. p. with the salt from 6-hydroxyindazole-5-sulphonic acid 226° (regenerated a hydroxyindazolesulphonic acid similar to 6-hydroxyindazole-5-sulphonic acid).

5-Hydroxyindazole-4-sulphonic acid. 5-Hydroxyindazole (13·5 g.) was added to 100% sulphuric acid (50 g.) with stirring at 20—30° during ½ hr., then stirred at 95—100° for 1 hr., poured on ice (50 g.) and water (100 c.c.) and kept for ½ hr. The pale grey crystals (17·5 g.) were recrystallised from water (Found : C, 38·8; H, 2·9; N, 13·0; S, 15·1%). The *product* did not couple and gave a reddish-mauve colour with ferric chloride. The *S*-*p*-chlorobenzylthiuronium salt had m. p. 215°.

6-Aminoindazole-7-sulphonic acid. 6-Hydroxyindazole (32 g.) was heated in a stainless-steel autoclave with 40% sodium hydrogen sulphite solution (45 g.) and ammonia (*d* 0·88; 300 c.c.) at 150—160° with stirring for 6 hr., then filtered at 75°, and the filtrate was evaporated to dryness under reduced pressure. The solid residue was dissolved in water (300 c.c.) and acidified with hydrochloric acid, and sulphur dioxide was boiled off. The solution was filtered and the filtrate neutralised to litmus with sodium hydroxide solution and cooled. The *product* (45%) was dissolved in dilute sodium carbonate solution, treated with carbon, and recovered by sulphuric acid as grey crystals (Found : N, 19·5%). It absorbed one equiv. of nitrous acid and did not couple in dilute acetic acid.

5-Aminoindazole-4-sulphonic acid. Amination of 5-hydroxyindazole-4-sulphonic acid as for 6-hydroxyindazole-7-sulphonic acid and purification of the product by carbon in alkaline solution, acidification, and crystallisation gave an *acid* (40·5%) (Found : C, 39·4; H, 3·2; N, 19·7; S, 14·7%), which absorbed 1 equiv. of nitrous acid and did not couple in dilute acetic acid.

7-Amino-6-hydroxyindazole-4-sulphonic acid (cf. Fieser, *J. Amer. Chem. Soc.*, 1926, **48**, 1103). 6-Hydroxyindazole (67 g.), dissolved in water (320 c.c.) and 32% sodium hydroxide solution (66 g.), was added with good stirring to 10% sulphuric acid (250 g.) and ice (250 g.). To the resulting fine suspension (alkaline to Brilliant Yellow) was added sodium nitrite (35 g.). After 5 minutes' stirring half of a solution of sulphuric acid (30 g.) in water (320 g.) was added during ½ hr. and the remainder during 2 hr., the temperature being held below 7° by addition of ice. After being stirred in an ice-bath overnight the nitroso-suspension was neutralised to Congo-red by sodium acetate crystals (20 g.), and 40% sodium hydrogen sulphite solution (312 g.) was added at 8°. Stirring was continued for ½ hr., the temperature being allowed to rise to 20°. After filtration, the solution (3 l.) was stirred at 40° while copper sulphate (5 g.) and concentrated sulphuric acid (120 g.) in water (300 c.c.) were added, the temperature rising 50°. After 10 minutes' stirring the mixture was kept for 24 hr., cooled to 10°, and filtered. The *acid* (crude, 80 g.) was purified by carbon, etc., forming cream needles (Found : N, 18·1. $C_7H_7O_4N_3S$ requires N, 18·3%).

A neutral suspension of this product (32 g.) was stirred with a solution of hydrated copper sulphate (0·3 g.) in water (50 c.c.) at 17°. Sodium nitrite (11·6 g.) was added. The temperature rose to 40°, and ice was added to reduce it to 18°; green prisms of the diazo-compound then began to separate. After ½ hour's stirring 10% sodium chloride solution (100 c.c.) was added, and the diazo-compound was filtered off, washed with 10% sodium chloride solution (50 c.c.), suspended in water (200 c.c.), and acidified with hydrochloric acid. The precipitate was washed with water (100 c.c.) and dried at 40—50° under reduced pressure (28 g.). The diazo-compound coupled in a similar manner to 1-diazo-2-naphthol-4-sulphonic acid.

4-Amino-5-hydroxyindazole-7-sulphonic acid. In the manner last described, 5-hydroxyindazole gave *4-amino-5-hydroxyindazole-7-sulphonic acid* (47%) as fawn needles (Found : N, 17·9%), which was very readily oxidised in air. Diazotisation as just described required working in nitrogen and total darkness.

4-Aminoindazole-6-sulphonic acid. 4-Methyl-5-nitrometanilic acid (116 g.; supplied by Mr. F. Hall) was suspended in glacial acetic acid (2·5 l.) and stirred at 15°. 40% Sodium nitrite solution (88 c.c.) was added all at once and stirring at 18—20° continued overnight.

The acetic acid was distilled off below 100° under reduced pressure. The residual solid (148 g.) was dissolved in hot water (400 c.c.) and added during 2 hr. to iron borings (40—60 mesh; 200 g.), ferrous chloride (14 g.), and water (800 c.c.) with stirring at 90—95° in an iron vessel. After a further 2 hours' stirring at 90—95° in presence of soluble iron, reduction was complete. Soluble iron was removed by the addition of sodium carbonate, and the iron sludge filtered off and repeatedly extracted with hot water. The combined filtrates (1·7 l.) were acidified with sulphuric acid and cooled. The crystalline *amino-acid* (73·5%) was purified by treatment with carbon in alkaline solution and precipitation with sulphuric acid as fawn plates (Found: N, 19·2%). The product reacted with one equiv. of nitrous acid and coupled in acetic acid solution with diazo-compounds.

4-*Hydroxyindazole*-6-*sulphonic acid*. 4-Aminoindazole-6-sulphonic acid (72·4 g.) was heated in an enamel-lined autoclave with 4% sulphuric acid (420 c.c.) at 175—180° for 10 hr. The dry sodium salt (108 g.), obtained as above *via* the calcium salt, was stirred with 36% hydrochloric acid (110 c.c.) and water (1 l.) for 10 min. The resulting *acid* (45 g.), purified as in the preceding case, formed pale brown needles (Found: N, 12·7. $C_7H_6O_4N_2S$ requires N, 13·1%), was soluble in water, coupled with one equiv. of diazotised *p*-chloroaniline (orange dye), and gave a brown precipitate with ferric chloride.

The author thanks Dr. H. A. Piggott for his interest and encouragement, Mr. A. Dixon for assistance with analyses and preparative work, Mr. R. Rothwell for microanalyses, Dr. R. H. Peters for ultraviolet absorption spectra, and Mr. F. Hall and Mr. E. G. Bainbridge for some of the starting materials.

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The Structure of Cyperone. Part IV. The Synthesis of (Natural) (+)-α-Cyperone, its Enantiomorph, and an Epimer.*

By R. Howe and F. J. McQuillin.

[Reprint Order No. 6216.]

The structure and configuration (IX) for natural (+)-α-cyperone have been confirmed by synthesis of its (+)- and (−)-form.

It was shown in Part III,* from a comparison with a synthetic ketone (IV), and its derivatives, that (+)-α-cyperone must have the absolute configuration (IX). The synthetic ketone (IV) was obtained by condensation of (−)-dihydrocarvone (I) with diethylmethyl-3-oxopentylammonium iodide. The ketol (II) which formed the principal product and could be dehydrated to give (IV), was accompanied by a mixture of dehydro-ketones regarded as (IV) and (III). The latter should represent (−)-α-cyperone.

A parallel series of products, (VII), (VIII), and (IX) has now been prepared from (+)-dihydrocarvone (VI).

The mixtures of dehydro-ketones (III) and (IV), and (VIII) and (IX), were conveniently separated *via* their oximes, the derivative of (+)-α-cyperone and its enantiomorph being the higher-melting and less soluble. Direct chromatography of the ketones on alumina was relatively ineffective.

The oximes were hydrolysed by oxalic acid in aqueous methanol in the presence of light petroleum. Continuous extraction of the ketone into the second phase largely avoids acid-induced isomerisation and contamination of the product with the corresponding β-cyperones (V) and (X). Any small amount of β-cyperone formed was removed by chromatography and in this way (+)-α-cyperone (IX) and its enantiomorph (III) were obtained in a state of purity. These ketones have been isomerised by sulphuric acid to the corresponding (+)- and (−)-β-cyperones (X) and (V).

With the preparation of the (−)-dehydro-ketone (VIII), following the methods of

* Part III, *J.*, 1955, 528.

Part III, all the possible isomers in this series have now been obtained. It is suggested that the compounds (IV) and (VIII) may be conveniently referred to as (+)- and (−)-6-*epi*-α-cyperones, and that in systematic nomenclature the 6-alkyl substituent may be designated α and β as in the sterol system.

The infrared and ultraviolet absorption spectra of the synthetic (+)-α-cyperone (IX) were identical with those of the natural ketone, and different from those of the (+)-6-*epi*-

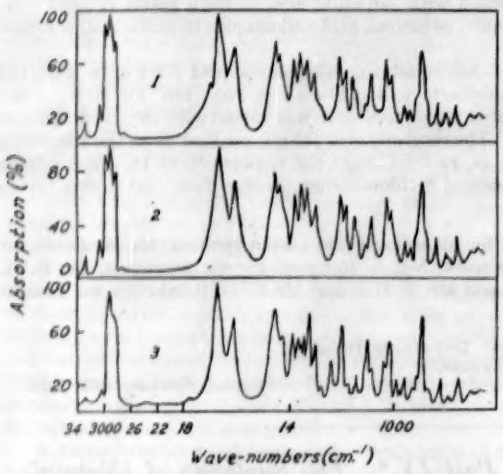


FIG. 1. *Infrared spectra of* (1) *natural* (*C.S. No.* 215) *and* (2) *synthetic* (+)-α-*cyperone* (*C.S. No.* 216) *and* (3) (+)-6-epi-α-*cyperone* (*C.S. No.* 217).*

* Larger copies of these spectra have been deposited with the Chemical Society. Photocopies, price 3*s.* 0*d.* per copy per spectrum, may be obtained on application, quoting the C.S. Nos. to the General Secretary, The Chemical Society, Burlington House, Piccadilly, London, W.1.

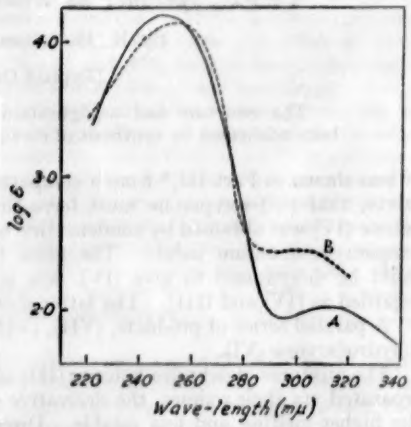
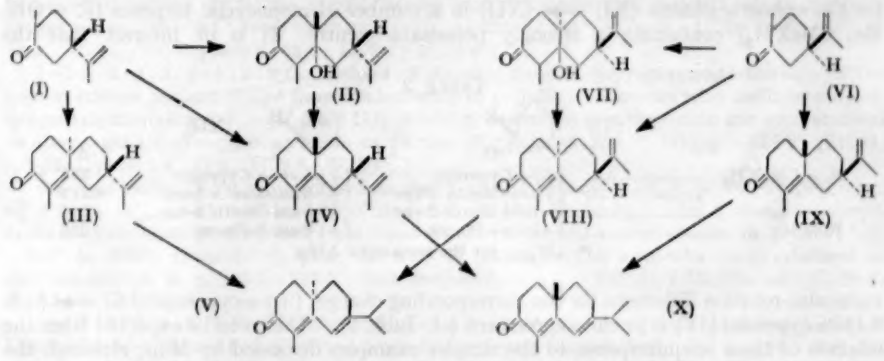


FIG. 2. *Ultraviolet spectra of* (*A*) *natural and synthetic* (+)-α-*cyperone and* (*B*) (+)-6-epi-α-*cyperone.*

ketone (IV) (cf. Figs. 1 and 2). The ultraviolet absorption maximum for the 6-*epi*-cyperones is moved by 3 mμ towards longer wavelengths and the intensity is somewhat reduced relative to the absorption of ketones of the natural series. Steric compression due to the axial *iso*propenyl group, which will raise the energy level of the ground state, would be expected to be relatively less in the excited state of the molecule. The main differences in the infrared spectra are summarised in Table 1 : in the *epi*-series certain additional hydrogen deformation frequencies, probably associated with the 6-hydrogen atom, and additional skeletal vibration frequencies are observed.

The oximes of natural and synthetic (+)-α-cyperone gave identical *X*-ray powder photographs.

The natural and the synthetic ketones are compared in Table 2. The synthetic ketones, and their semicarbazones and 2 : 4-dinitrophenylhydrazones, were chromatographed specimens. The correspondence in physical properties leaves no doubt that natural



(+)-α-cyperone has the structure and configuration (IX). The close agreement excludes the possibility of anything beyond minute amounts of any other isomer in the ketone isolated from natural sources and supports this conclusion reached earlier on other grounds (Cardwell and McQuillin, *J.*, 1955, 526). Only two points require comment. The rotation of natural (+)-α-cyperone semicarbazone has been redetermined. Bradfield, Hedge, Rao, Simonsen, and Gillam (*loc. cit.*) give the melting point of the 2 : 4-dinitrophenylhydrazone of the natural ketone as 210°; Barton and Tarlton (*loc. cit.*) give 188—190° for a chromatographed specimen. Our product, m. p. 205°, was homogeneous on chromatography and gave no evidence in the ultraviolet spectrum of the presence of the derivative of

TABLE 1. *Absorption peaks* ($cm.^{-1}$).

(+)-α-Cyperone	1351		1181	1106	1007	937	837
	1322			1083			
(+)-6-*epi*-α-Cyperone	1353	1232		1091	1033	983	819
	1347			1073		973	
	1333					928	
	1315					915	

TABLE 2.

	Natural	Synthetic (+)	Synthetic (−)		Natural	Synthetic (+)	Synthetic (−)
	Ketones				Semicarbazones		
n_D^{17}	1·5292 [a]	1·5294	1·5288	M. p.	215—216° [c]	215—216°	215—216°
$[\alpha]_{5461}$	+119·2° [b]	+115·4°	−115·9°	$[\alpha]_{5461}$	+244°	+231°	−227°
$\lambda_{max.}$ (mμ) [c]	250·0	249·5	249·5	$\lambda_{max.}$ (mμ) [c]	270 [c]	272	—
log ε	4·17	4·21	4·21	log ε	4·32	4·48	—
	Oximes				2 : 4-Dinitrophenylhydrazones		
M. p.	150·5° [c]	150·5°	150·5°	M. p.	210° [c]	205°	205°
$[\alpha]_{5461}$	+134° [c]	+134°	−134°	$[\alpha]_{5461}$	+414° [d]	+387°	−395°
$\lambda_{max.}$ (mμ) [c]	244 [c]	244	—	$\lambda_{max.}$ (mμ) [f]	395 [d]	395	395
log ε	4·25	4·28	—	log ε	4·47	4·46	4·45

[a] Bradfield, Hegde, Rao, Simonsen, and Gillam, *J.*, 1936, 667. [b] Cf. Part II, *J.*, 1955, 526. [c] Cf. Part I, *J.*, 1951, 716. [d] Barton and Tarlton, *J.*, 1954, 3492. [e] In EtOH. [f] In $CHCl_3$.

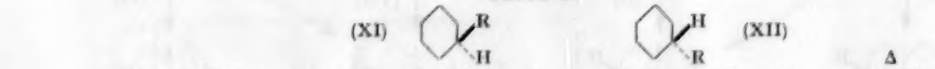
β-cyperone. Sharp melting points over a relatively wide range of values are, however, characteristic of a number of 2 : 4-dinitrophenylhydrazones (cf., *e.g.*, Woodward, Sondheimer, Taub, Heusler, and McLamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4226). In solution the different samples show essentially identical properties (rotation and ultraviolet absorption). The difference in melting point must be ascribed to differences in crystal habit.

The properties of (−)-6-*epi*-α-cyperone (VIII) and of (−)-β-cyperone (V) and their

derivatives agreed closely with those for the (+)-enantiomorphs previously reported (cf. Experimental section and Part III).

Mills (*J.*, 1952, 4976) drew attention to the large positive molecular-rotation difference for the epimeric change (XI) ⟶ (XII) in a number of monocyclic terpenes (R = OH, Me, CMe:CH_2) containing a strongly polarisable centre. It is of interest that the

TABLE 3.



			Δ
R = CMe:CH_2	(+)-α-Cyperone	(+)-6-*epi*-α-Cyperone	+238° *
,,	(+)-*cis*-Menth-2-ene	(+)-*trans*-Menth-2-ene	+119
,,	(−)-*cis*-Menth-2-ene	(+)-*trans*-Menth-2-ene	+245
R = Me	(−)-*cis*-δ-Pinene	(+)-*trans*-δ-Pinene	+226

* ΔM_{5461}, for the remainder ΔM_D.

molecular-rotation difference for the corresponding change, (+)-α-cyperone (IX) ⟶ (+)-6-*epi*-α-cyperone (IV) is in close agreement (cf. Table 3). This is to be expected from the relation of these sesquiterpenes to the simpler examples discussed by Mills, although the polarisable centres are differently located in these cases.

It is also of interest that the absolute stereochemistry of (+)-α-cyperone corresponds with that established for (+)-β-eudesmol (Woodward, Fürst, Riniker, Kalvoda, Arigoni, Jeger, and Gold, *J. Amer. Chem. Soc.*, 1954, **76**, 313) and for (−)-α-santonin (Woodward and Yates, *Chem. and Ind.*, 1954, 1391), and that in all these instances the 6-substituent adopts the thermodynamically more stable configuration.

EXPERIMENTAL

Ultraviolet spectra were measured on a Hilger Uvispectrometer. Infrared absorption spectra were measured on a Grubb–Parsons double-beam spectrometer on liquid films of 0·02-mm. thickness. Ultraviolet spectra and $[\alpha]_{5461}$ are for solutions in $CHCl_3$ unless otherwise stated.

Condensation of (+)-*Dihydrocarvone with Diethylmethyl-3-oxopentylammonium Iodide.*—(+)-Dihydrocarvone (45 g.) in ether (200 c.c.) was converted into the sodio-derivative by sodamide (12·7 g.) under ether (200 c.c.). Diethylmethyl-3-oxopentylammonium iodide (86 g.) in dry pyridine (90 c.c.) was then added, and the mixture stirred at 0° for 6 hr. and then refluxed for 5½ hr. Water was then added and the ether extract washed free from pyridine and dried. Distillation gave (+)-dihydrocarvone (9 g.), followed by a fraction, b. p. 115—130°/0·2 mm. (42·8 g.), which solidified and by means of light petroleum gave (+)-*decahydro*-10-*hydroxy*-4 : 9-*dimethyl*-3-*oxo*-6β-iso*propenylnaphthalene* (23 g.), m. p. 106°, $[\alpha]_{5461}$ +54° (*c*, 3·0) (Found : C, 76·0; H, 10·1. $C_{15}H_{24}O_2$ requires C, 76·3; H, 10·2%). Redistillation of the non-crystalline material gave further (+)-ketol (2 g.) and the residue was chromatographed on alumina. Elution with light petroleum (b. p. 60—80°) gave fractions, (*a*) b. p. 104—106°/0·3 mm. (5·35 g.), n_D^{20} 1·5260, $[\alpha]_{5461}$ −10° (*c*, 5·95) (Found : C, 82·5; H, 10·2. Calc. for $C_{15}H_{22}O$: C, 82·6; H, 10·1%), (*b*) b. p. 106—108°/0·3 mm. (2·55 g.), n_D^{20} 1·5285, $[\alpha]_{5461}$ −62° (*c*, 5·2) (Found : C, 82·3; H, 10·35%), and (*c*) the (+)-ketol (1 g.), m. p. 105°.

(+)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-*Octahydro*-4 : 9-*dimethyl*-3-*oxo*-6β-iso*propenylnaphthalene.*—(i) The combined fractions (*a*) and (*b*) above were converted into the oxime. Repeated crystallisation from methanol gave (+)-α-*cyperone oxime* as needles (2 g.), m. p. and mixed m. p. 150·5°, $[\alpha]_{5461}$ +133·5° (EtOH ; *c*, 1·09) (Found : C, 77·5; H, 9·8; N, 6·2. $C_{15}H_{23}ON$ requires C, 77·25; H, 9·9; N, 6·0%).

(ii) This oxime (1·25 g.) in methanol (55 c.c.), water (25 c.c.), light petroleum (b. p. 60—80° ; 20 c.c.) was refluxed for 22 hr. with oxalic acid (3 g.) and 40% aqueous formaldehyde (15 c.c.). Water was added and the light petroleum layer washed and dried. Chromatography of the product on alumina with light petroleum (b. p. 60—80°) gave (+)-α-*cyperone* as a colourless oil, b. p. 96—97°/0·2 mm., n_D^{17} 1·5294, $[\alpha]_{5461}$ +115·4° (*c*, 1·3) (Found : C, 82·7; H, 10·1%). The 2 : 4-dinitrophenylhydrazone formed red needles, m. p. 204°, from ethyl acetate. Chromatography of the product on alumina with benzene–light petroleum (b. p. 40—60°) (1 : 3), and collection of fractions of maximal absorption at 395 mμ gave (+)-α-*cyperone* 2 : 4-*dinitrophenylhydrazone* as scarlet prisms, m. p. and mixed m. p. 205°, from chloroform–di*iso*propyl ether,

$[\alpha]_D$ +387° (*c*, 0·088) (Found: C, 62·9; H, 6·7; N, 13·9. $C_{21}H_{26}O_4N_4$ requires C, 63·3; H, 6·5; N, 14·1%). The *semicarbazone* crystallised as irregular prisms, m. p. and mixed m. p. 215—216°, from methanol, $[\alpha]_{5461}$ +233° (*c*, 1·9). After chromatography on alumina in benzene–chloroform (1 : 3) the semicarbazone was recovered and crystallised as irregular prisms, m. p. 215—216°, from methanol, $[\alpha]_{5461}$ +231° (*c*, 1·47) (Found: C, 70·1; H, 9·2; N, 15·2. $C_{16}H_{25}ON_3$ requires C, 69·8; H, 9·1; N, 15·3%).

(−)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-*Octahydro*-4 : 9-*dimethyl*-3-*oxo*-6α-iso*propenylnaphthalene*.—(i) The non-crystalline product (14 g.) from condensation of (−)-dihydrocarvone with diethylmethyl-3-oxopentylammonium iodide (cf. Part III), similarly converted into the oxime and recrystallised as above, gave (−)-α-*cyperone oxime* as needles (2 g.), m. p. 150·5°, $[\alpha]_{5461}$ −133·9° (EtOH, *c*, 1·35) (Found: C, 77·2; H, 9·8; N, 5·8%).

(ii) This oxime (1·1 g.), hydrolysed as above, gave (−)-α-*cyperone*, b. p. 96—98°/9·2 mm., n_D^{17} 1·5288, $[\alpha]_{5461}$ −115·9° (*c*, 1·6) (Found: C, 82·85; H, 10·3%). Its 2 : 4-*dinitrophenylhydrazone*, chromatographed and crystallised as above, formed scarlet prisms, m. p. 205°, $[\alpha]_D$ −395° (*c*, 0·036) (Found: C, 63·3; H, 6·8; N, 13·8%). The *semicarbazone* crystallised as irregular prisms, m. p. 215·5—216·5°, from methanol, $[\alpha]_{5461}$ −227° (*c*, 1·75) (Found: C, 69·9; H, 9·5; N, 15·3%).

(−)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-*Octahydro*-4 : 9-*dimethyl*-3-*oxo*-6β-iso*propenylnaphthalene*.—(*a*) (+)-Decahydro-10-hydroxy-4 : 9-dimethyl-3-oxo-6β-*iso*propenylnaphthalene (5 g.) in alcoholic potassium hydroxide (10%; 50 c.c.) was refluxed under nitrogen for 8 hr. The mixture was then cooled, diluted, and neutralised with dilute hydrochloric acid. The product, isolated in ether, on distillation gave (−)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-*octahydro*-4 : 9-*dimethyl*-3-*oxo*-6β-iso*propenylnaphthalene* as a pale yellow oil, b. p. 102—104°/0·25 mm. (4·3 g.), n_D^{20} 1·5340, $[\alpha]_{5461}$ −225° (*c*, 5·0), $\lambda_{max.}$ 252·5 mμ (log ε 4·16) (EtOH) (Found: C, 82·5; H, 10·2%). The 2 : 4-*dinitrophenylhydrazone* formed red needles, m. p. 202°, from ethyl acetate (Found: C, 63·3; H, 6·1; N, 13·8%). The *oxime* formed flattened needles, m. p. 89·5—90° (from methanol–water), $[\alpha]_{5461}$ −177° (EtOH, *c*, 2·7) * (Found: C, 77·1; H, 10·0; N, 6·4%). The *semicarbazone* formed prisms, m. p. 176° (from methanol), $[\alpha]_{5461}$ −267° (*c*, 2·0) (Found: C, 70·0; H, 8·9; N, 15·6%).

(*b*) (+)-Decahydro-10-hydroxy-4 : 9-dimethyl-3-oxo-6β-*iso*propenylnaphthalene (1·5 g.) in ethanol (25 c.c.) was treated with concentrated hydrochloric acid (2·5 c.c.). After 8 days, water was added, and the solution neutralised with sodium hydrogen carbonate. The bulk of the ethanol was removed in a vacuum and the oil extracted with ether. The oil after chromatography on alumina with light petroleum (b. p. 60—80°) gave (−)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-octahydro-4 : 9-dimethyl-3-oxo-6β-*iso*propenylnaphthalene, b. p. 98°/0·2 mm. (1 g.), n_D^{20} 1·5337, $[\alpha]_{5461}$ −228° (*c*, 1·2) (Found: C, 82·7; H, 10·3%). This material gave a 2 : 4-dinitrophenylhydrazone, oxime, and semicarbazone identical with those prepared above.

(+)-1 : 2 : 3 : 7 : 8 : 9-*Hexahydro*-4 : 9-*dimethyl*-3-*oxo*-6-iso*propylnaphthalene*.—(+)-α-Cyperone (0·25 g.) was treated with ice-cold sulphuric acid (50% v/v; 3·5 c.c.). After 6 hr. ice and water were added. The oil isolated with ether gave (+)-1 : 2 : 3 : 7 : 8 : 9-hexahydro-4 : 9-dimethyl-3-oxo-6-*iso*propylnaphthalene, b. p. 95°/0·2 mm., n_D^{20} 1·5620, $[\alpha]_{5461}$ +681° (*c*, 2·1), $\lambda_{max.}$ 300·5 mμ (log ε 4·49) (EtOH) (cf. Part III) (Found: C, 82·3; H, 10·35%). The 2 : 4-*dinitrophenylhydrazone* formed plates, m. p. 230—231° (from ethyl acetate), $\lambda_{max.}$ 417 mμ (log ε 4·50) (Found: C, 62·8; H, 6·5; N, 14·5%).

(−)-1 : 2 : 3 : 7 : 8 : 9-*Hexahydro*-4 : 9-*dimethyl*-3-*oxo*-6-iso*propylnaphthalene*.—(*a*) (+)-Decahydro-10-hydroxy-4 : 9-dimethyl-3-oxo-6β-*iso*propenylnaphthalene (1·5 g.) was treated with ice-cold sulphuric acid (50% v/v; 20 c.c.). After 6 hr. ice and water were added. The oil isolated with ether gave (−)-1 : 2 : 3 : 7 : 8 : 9-*hexahydro*-4 : 9-*dimethyl*-3-*oxo*-6-iso*propylnaphthalene* as a pale yellow oil, b. p. 95—98°/0·25 mm. (1·3 g.), n_D^{20} 1·5619, $[\alpha]_{5461}$ −688° (*c*, 2·7), $\lambda_{max.}$ 301 mμ (log ε 4·40) (EtOH) (Found: C, 82·6; H, 10·3%). The 2 : 4-*dinitrophenylhydrazone* formed plates, m. p. 231—232° (from ethyl acetate), $\lambda_{max.}$ 417 mμ (log ε 4·50) (Found: C, 63·4; H, 6·6; N, 13·7%). The *oxime* formed needles, m. p. 139° (from methanol), $[\alpha]_{5461}$ −320° (EtOH *c*, 1·2) (Found: C, 77·1; H, 9·7; N, 5·7%). The *semicarbazone* formed slightly yellow plates (photochromic), m. p. 208° (from methanol), $[\alpha]_{5461}$ −399° (*c*, 1·9) (Found: C, 70·0; H, 9·4; N, 15·05%). (*b*) (−)-α-Cyperone (0·15 g.), treated with ice-cold sulphuric acid (50% v/v; 2 c.c.) and re-isolated after 6 hr. as above, gave (−)-1 : 2 : 3 : 7 : 8 : 9-hexahydro-4 : 9-dimethyl-3-oxo-6-*iso*propylnaphthalene, b. p. 94—96°/0·2 mm., n_D^{20} 1·5622, $[\alpha]_{5461}$ −679° (*c*, 0·7) (Found: C,

* The rotation of the (+)-enantiomorph of this oxime was given in Part III (*loc. cit.*) as +233°. This should read +178°.

82·8; H, 10·2%), characterised as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 231° (Found: C, 63·2; H, 6·7; N, 14·1%).

One of us (R. H.) is indebted to the Department of Scientific and Industrial Research for an award. We thank Sir John Simonsen, F.R.S., for specimens, Mr. R. E. Dodd for the infrared determinations, and Dr. K. H. Jack for *X*-ray photographs.

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Infrared Spectra and Crystallinity. Part I. Polyesters.

By W. H. T. DAVISON and P. J. CORISH.

[Reprint Order No. 6004.]

The infrared spectra of crystalline and amorphous aliphatic polyesters show marked differences. The spectra of the crystalline materials are consistent with an approximately planar *trans*-configuration of the acid portion of the chains; this configuration is not shown in the molten state.

The acid portions of the molten polyesters are considered to have a continuous random configuration, rather than to consist of discrete rotational isomers.

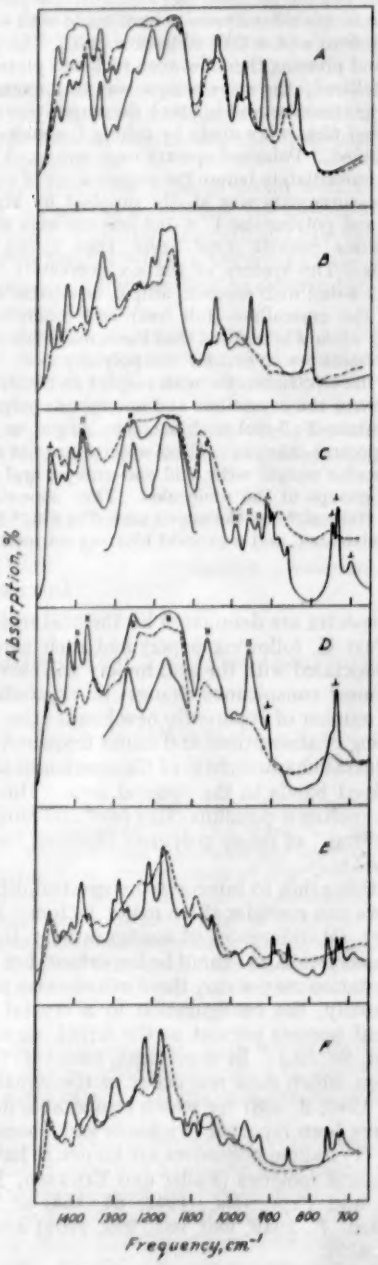
THE infrared spectra of many compounds show appreciable differences between the crystalline and in the amorphous state (Richards and Thompson, *Proc. Roy. Soc.*, 1948, *A*, **195**, 1); *e.g.*, *n*-alkyl bromides (Brown and Sheppard, *Trans. Faraday Soc.*, 1954, **50**, 535) and *n*-paraffins (Brown, Sheppard, and Simpson, *Discuss. Faraday Soc.*, 1950, **9**, 261; Sheppard and Simpson, *Quart. Reviews*, 1953, **7**, 19) show more bands in the liquid, due to additional rotational isomers. On the other hand, long-chain monocarboxylic acids (Sinclair, McKay, and Jones, *J. Amer. Chem. Soc.*, 1952, **74**, 2570) show fewer bands in the liquid, and this is also attributed to the presence of rotational isomers, whose absorptions are not resolved. Many polymers also show spectral changes on crystallising (Nichols, *J. Appl. Phys.*, 1954, **25**, 840; Sutherland and Jones, *Discuss. Faraday Soc.*, 1950, **9**, 281; Mochel and Hall, *J. Amer. Chem. Soc.*, 1949, **71**, 4082). Polymorphic modifications also may give rise to spectral differences (Kendall, *Analyt. Chem.*, 1953, **25**, 382; Sutherland and Jones, *loc. cit.*).

The extent to which the spectrum of a compound may depend upon the state of aggregation and even polymorphic form has not always been sufficiently realised. When such differences have been noted, they have usually been avoided by working in dilute non-polar solutions (*e.g.*, Cole, *Chem. and Ind.*, 1954, 661). However, the conscious use of these differences can assist in structural diagnosis and identification. Furthermore, an improved understanding of the complex relationship of vibrational spectra and state of aggregation would assist in the interpretation of the spectra of complex molecules; conversely, it should increase our knowledge of the structure of crystals and of liquids.

We now report and discuss the spectra of crystalline and amorphous aliphatic polyesters; since the completion of this work, Coffey and Meyrick ("Third Rubber Technology Conference," London, 1954) have reported and used the appearance of crystallinity bands in polyethylene sebacate and adipate, but without discussion of their origin. The dicarboxylic acids and their nonpolymeric esters will be the subject of future publications in this series.

EXPERIMENTAL

The polyesters were made on a 10—15 g. scale by Carothers and Arvin's method (*J. Amer. Chem. Soc.*, 1929, **51**, 2560), and the condensation continued until a crystallisable polyester was obtained of molecular weight about 2000. Several other samples of polyethylene adipate from various sources and of different molecular weight had essentially the same spectra. Normally, the polyesters had hydroxyl end-groups, but propane-1 : 2- and butane-2 : 3-diols gave products of low molecular weight with acid end-groups.



Infrared spectra of polyesters.

(*A*) Polyethylene succinate.
(*B*) Polybutane-1 : 4-diol succinate.
(*C*) Polyethylene adipate.
(*D*) Polybutane-1 : 4-diol adipate.
(*E*) Polyethylene sebacate.
(*F*) Polybutane-1 : 4-diol sebacate.

Note : Full-line (——), crystalline.
Broken line (– – –), molten.
∥ = parallel dichroism.
⊥ = perpendicular dichroism.

In (*A*), (*C*), and (*D*), spectra of thinner crystalline samples in KCl discs are shown in part.

Some of the polyesters were purified by solution in chloroform and precipitation with light petroleum, but the physical and spectroscopic properties were not thereby appreciably altered.

Spectroscopic measurements were made with a Grubb-Parsons S3 spectrometer (with sodium chloride prism) and a DBl radiation unit. The polyesters were prepared for examination by melting and pressing them between rock-salt plates. Spectra were measured after the materials had crystallised; the same sample was then examined molten and again after recrystallisation. The last spectrum served to check decomposition or change of cell thickness.

Oriented films were made by rolling the molten polyesters between silver chloride sheets as they solidified. Polarised spectra were measured by using a 5-plate silver chloride transmission polariser immediately before the entrance slit of the monochromator. The polariser used for the initial measurements was kindly supplied by Mr. H. A. Willis. Polyethylene succinate and adipate, and polybutane-1 : 4-diol adipate were also measured crystalline in pressed potassium chloride discs (Schiedt, *Appl. Spect.*, 1953, **7**, 75.)

Results.—The spectra of the six polyesters from the condensation of ethylene glycol or butane-1 : 4-diol with succinic, adipic, or sebacic acid are shown in the Figure. The differences between the crystalline (full line) and amorphous (broken line) spectra are very marked, especially when it is realised that these materials do not completely crystallise.

Dichroisms are shown for the polyadipates; " perpendicular " or " parallel " refers to the plane of the electric vector with respect to the direction of rolling.

Spectra of the crystalline and amorphous polyesters from the condensation of propane-1 : 2-diol or butane-2 : 3-diol with succinic, adipic, or sebacic acid were also measured and showed similar spectral changes. These spectra are not reported in detail, since the polyesters were of low molecular weight with acid end-groups, and the crystallinity could be associated with the acid end-groups of the molecules. They showed the characteristic crystallinity bands at *ca.* 890 and 805 cm.$^{-1}$ for the succinates, 734 cm.$^{-1}$ for the adipates, and 855, 755, and 722 cm.$^{-1}$ for the sebacates, and a general blurring on melting.

Discussion

The spectra are dominated by the acid moiety; this is confirmed by the spectra of the acids (Part II, following paper) and their simple esters, and a detailed discussion of the bands associated with the acid moiety will therefore be the subject of a later publication.

The most conspicuous changes on crystallisation are in the 700—900 cm.$^{-1}$ region, in which a number of apparently new bands arise. In other regions, the changes are a general sharpening of absorptions and minor frequency shifts.

A general characteristic of the spectra of molten polyesters is the absence of sharp or well-defined bands in the skeletal area. This is in contrast to the increased number of bands in molten *n*-paraffins (Sheppard and Simpson, *loc. cit.*) but similar to the loss of bands on " melting " of many polymers (Nichols, *loc. cit.*) and monocarboxylic acids (Sinclair *et al.*, *loc. cit.*).

In attempting to interpret the spectral differences between crystalline and amorphous states, we can consider three major factors: (*a*) differences of association, *e.g.*, hydrogen-bonding; (*b*) differences of configuration; (*c*) intermolecular interactions. In the polyesters, association (*a*) cannot be important, but, since there are a number of C–C bonds about which rotation may occur, there are obvious possibilities of configurational differences (*b*).

Normally, the configuration in a crystal is one of the more energetically favoured rotational isomers present in the liquid, as in the case of the *n*-paraffins (Sheppard and Simpson, *loc. cit.*). In some cases, however, the crystal packing enforces a molecular configuration which does not occur in the liquid, *e.g.*, in diphenyl (Bastiansen, *Acta Chem. Scand.*, 1949, **3**, 408) for which remarkable differences between the spectra of liquid and solid have been reported (Richards and Thompson, *loc. cit.*).

The crystalline polyesters are known to have approximately planar *trans*-configurations of their acid moieties (Fuller and Erickson, *J. Amer. Chem. Soc.*, 1937, **59**, 344; Fuller, Frosch, and Pape, *ibid.*, 1942, **64**, 154) as have the dicarboxylic acids (Morrison and Robertson, *J.*, 1949, 980, 987, 993, 1001) and *n*-paraffins (Muller, *Proc. Roy. Soc.*, 1928, *A*, **120**, 437).

In the crystalline state the polyesters, dicarboxylic acids, and *n*-paraffins show a band in the 800—720 cm.$^{-1}$ region which is reliably assigned (Sheppard and Simpson, *loc. cit.*) to

the out-of-plane rocking deformation of a *trans*-$[CH_2]_n$ chain ($\delta[CH_2]_n$). However, this band virtually disappears in the amorphous polyesters and dicarboxylic acids (Part II), showing the absence of this configuration. Calculations (Person and Pimental, *J. Amer. Chem. Soc.*, 1953, **75**, 532) have shown that this band is very sensitive to deviations from planarity.

The absence of the $\delta[CH_2]_n$ band in molten polyesters is contrary to previously published correlations (Colthup, *J. Opt. Soc. Amer.*, 1950, **40**, 397; Bellamy, "Infra-red Spectra of Complex Molecules," Methuen, 1954, pp. 13, 26) and emphasises that this band is only associated with an essentially planar *trans*-configuration.

Comparison of the spectra of molten polyesters with those of liquid *n*-paraffins with corresponding methylene chains shows that, unlike the *n*-paraffins, the molten polyesters do not exist in a few discrete rotational isomers. Even the energetically favoured planar configuration is practically non-existent. This implies either a lowering of the potential barriers to rotation or, more probably, increased forces tending to deform the polymer chains from the energetically-favoured *trans*-configurations.

The number of possible rotational isomers in the polyesters is too great to distinguish between a large number of discrete isomers and a continuous range of non-discrete configurations. In the simpler dicarboxylic acids (Part II), the evidence supports the conception of a continuous range of non-discrete configurations.

The 735, 748 cm.$^{-1}$ doublet in crystalline polyethylene adipate probably arises from intermolecular interactions of the $\delta[CH_2]_n$ vibration, as in the case of polyethylene (Rugg, Smith, and Wartman, *J. Polymer Sci.*, 1953, **11**, 1).

We thank the Dunlop Rubber Company for permission to publish this work.

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Infrared Spectra and Crystallinity. Part II. αω-Dicarboxylic Acids.*

By P. J. CORISH and W. H. T. DAVISON.

[Reprint Order No. 6005.]

Infrared spectra of the αω-dicarboxylic acids $CO_2H{\cdot}[CH_2]_n{\cdot}CO_2H$ with $n = 2$—8, 10, 14, and 16 have been measured from 3500 to 670 cm.$^{-1}$, with both crystalline and molten material. The spectra of crystalline material are consistent with an approximately planar *trans*-configuration of the $[CH_2]_n$ chain and association of the type (I) (p. 2434). On melting of the materials, however, the spectra change considerably, many bands blurring or disappearing. These changes are attributed to a break-up of the normal association and a loss of the planar configuration. It is considered that the molten acids adopt a continuous range of configurations rather than a number of discrete rotational isomers.

IN Part I * it was reported that amorphous aliphatic polyesters gave unusually ill-defined spectra, but that they showed sharp bands in the crystalline state. In particular the absorption at about 720 cm.$^{-1}$ (the rocking mode of a $[CH_2]_n$ chain) virtually disappeared on melting.

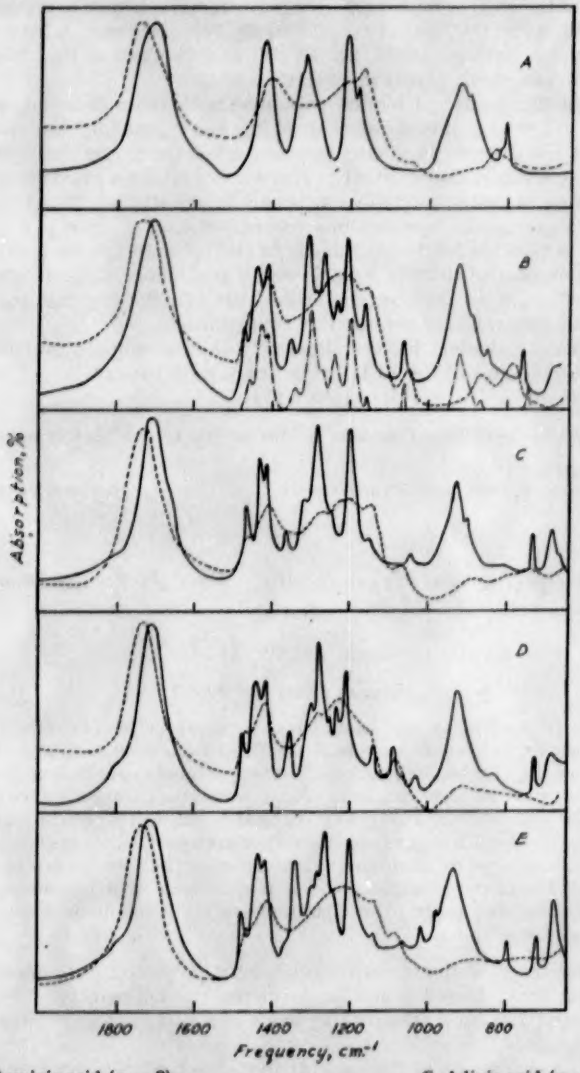
As the spectral changes on melting are attributed to configurational changes of the acid portion of the polyesters, the dicarboxylic acids themselves have now been examined.

Previous infrared studies of aliphatic dicarboxylic acids have been made by Flett (*J.*, 1951, 962) and Hadži and Sheppard (*Proc. Roy. Soc.*, 1953, *A*, **216**, 247). Adipic acid has also been studied with polarised radiation by Mann and Thompson (*ibid.*, 1948, *A*, **192**, 489) and by Kuratani (*J. Chem. Soc. Japan*, 1951, **72**, 924) who also examined succinic acid. In all these studies the acids were examined only in the crystalline state. After the

* Part I, preceding paper.

completion of this work, our attention was drawn to a paper on the spectra of dicarboxylic acids of $n = 3$—7 (Schonmann, *Helv. Phys. Acta*, **1943**, **16**, 343) in which spectral differences were reported for crystalline and liquid glutaric acid only.

FIG. 1. *Infrared spectra of dicarboxylic acids* ($CO_2H{\cdot}[CH_2]_n{\cdot}CO_2H$), *crystalline* (——) *and molten* (– – –)



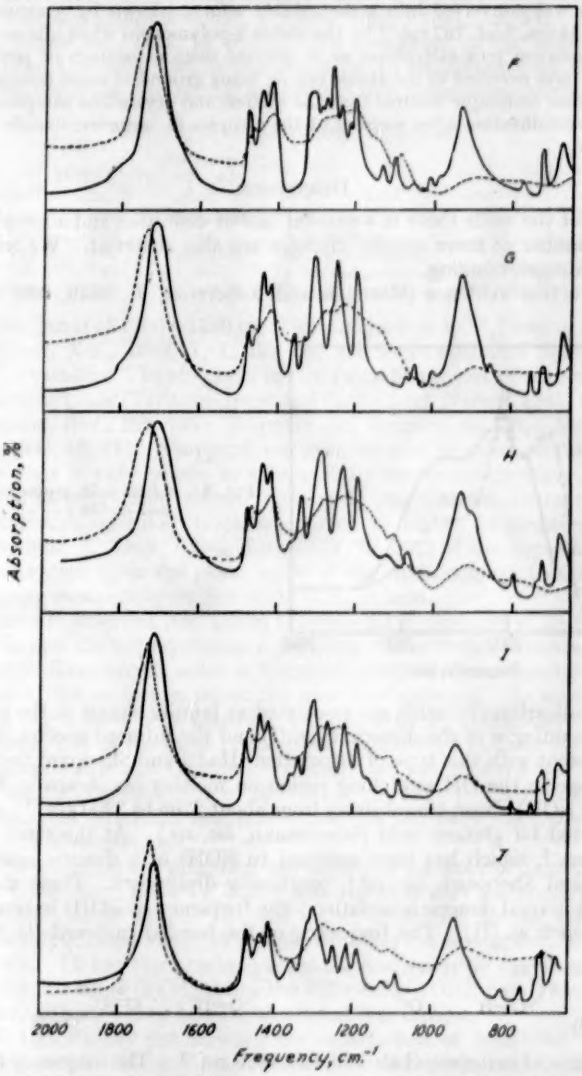
A, β-Succinic acid ($n = 2$).
B, β-Glutaric acid ($n = 3$) [chain-line (—·—) is of α-glutaric acid, displaced].
C, Adipic acid ($n = 4$).
D, Pimelic acid ($n = 5$).
E, Suberic acid ($n = 6$).

EXPERIMENTAL

The acids used were mostly good-quality commercial materials, whose m. p.s agreed satisfactorily with the literature. The acid with $n = 16$ was prepared by Dr. G. B. Barlow by a Kolbe synthesis.

Samples were originally prepared for spectroscopic measurement by squeezing when molten between rock-salt plates and allowing them to crystallise. The spectra of the molten materials were measured on the same cells at a temperature just above the m. p., a hot cell being used.

FIG. 2. *Infrared spectra of dicarboxylic acids* ($CO_2H{\cdot}[CH_2]_n{\cdot}CO_2H$), *crystalline* (——) *and molten* (– – –).



F, Azelaic acid ($n = 7$).
G, Sebacic acid ($n = 8$).
H, Dodecanedioic acid ($n = 10$).
I, Hexadecanedioic acid ($n = 14$).
J, Octadecanedioic acid ($n = 16$).

After recrystallisation, the spectra were re-measured to confirm that no decomposition had taken place. With succinic acid, some anhydride was formed. The acids (except $n = 16$) were re-measured in pressed discs of potassium chloride by means of a die of the type described by Ford and Wilkinson (*J. Sci. Instr.*, 1954, **31**, 338).

The spectra of the crystalline acids measured as pressed discs differed appreciably from those measured between rock-salt plates, particularly in showing a stronger 1435-cm.$^{-1}$ band. This was shown to be due to orientation in the samples recrystallised between plates, by re-measuring these at an inclination of 45° to the beam. Except for $n = 16$, all the spectra shown in Figs. 1 and 2 are of pressed disc samples.

Glutaric acid was converted into a metastable α-form (shown by a chain line in Fig. 1) with a band at 754 cm.$^{-1}$ (cf. 762 cm.$^{-1}$ for the stable β-polymorph) when allowed to recrystallise from the melt between rock-salt plates or in pressed discs of sodium or potassium chloride. This metastable form reverted to the stable one on being ground at room temperature.

The pressed-disc technique ensures that the molten and crystalline samples are of the same thickness. Recrystallisation after melting of the samples is, however, usually slow and sometimes incomplete.

Discussion.

On melting of the acids there is a general loss of definition and a broadening of all the bands, but a number of more specific changes are also observed. We will first consider those due to hydrogen-bonding.

X-Ray diffraction evidence (Morrison and Robertson, *J.*, 1949, 980, 987, 993, 1001)

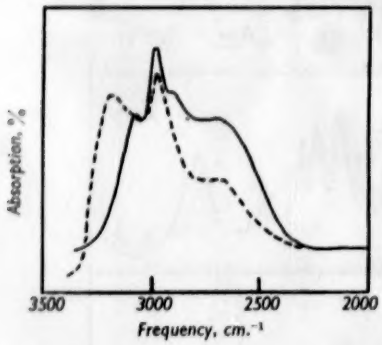
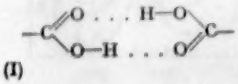
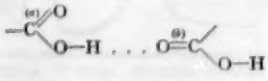


Fig. 3. *Adipic acid, crystalline* (——) *and molten* (– – –).

shows that the dicarboxylic acids are associated as infinite chains in the crystalline state; the hydrogen-bonding is of the dimeric type (I) and the infrared spectra of the crystalline acids are consistent with this type of association (Hadži and Sheppard, *loc. cit.*). There is a marked change in the OH stretching region on melting (as shown in Fig. 3 for adipic acid), the main ν(OH) absorption shifting from about 2700 to 3200 cm.$^{-1}$; a similar change has been reported for glutaric acid (Schonmann, *loc. cit.*). At the same time the strong band at 930 cm.$^{-1}$, which has been assigned to δ(OH) of a dimeric associated carboxyl group (Hadži and Sheppard, *loc. cit.*), practically disappears. These changes show the break-up of the normal dimeric association; the frequency of ν(OH) indicates a looser type of association such as (II). The frequency of the bonded carbonyl (*b*) would be similar



(I)



(II)

to that of adipic acid in *iso*propyl alcohol, *i.e.*, 1720 cm.$^{-1}$. The frequency for the unbonded carbonyl (*a*) would not be that for a monomeric acid but at a lower frequency owing to participation of the hydroxyl group in external hydrogen-bonding; *e.g.*, adipic acid in dioxan has an absorption at 1735 cm.$^{-1}$.

Carbonyl absorptions of acids in ether or dioxan are usually about 20 cm.$^{-1}$ lower than the monomeric bands in dilute solution in carbon tetrachloride (Davison, unpublished work); this shift is significantly greater that that due to normal solvent effects (Hartwell, Richards, and Thompson, *J.*, 1943, 1936). On melting, the carbonyl absorptions of the

dicarboxylic acids shift from 1700 to about 1730 cm.$^{-1}$; they become broad with evidence of complexity and are consistent with the loose type of association (II).

In the 1450-cm.$^{-1}$ region, the crystalline acids (except succinic) show three distinct bands, at 1475, 1435, and 1415 cm.$^{-1}$, which we assign respectively to a normal $\delta(CH_2)$ bending, a carboxyl vibration (Hadži and Sheppard, *loc. cit.*), and a $\delta(CH_2)$ bending perturbed by an adjacent carbonyl group (Francis, *J. Chem. Phys.*, 1951, **19**, 942; Jones, Cole, and Nolin, *J. Amer. Chem. Soc.*, 1952, **74**, 5662). The assignment of the 1435-cm.$^{-1}$ band to a different mode from the other two is confirmed by its dependence on orientation. Its absence in the molten acids confirms its assignment to a dimer-associated carboxyl group.

Table of $\delta[CH_2]_n$ *rocking frequencies.*

n	Acid	(cm.$^{-1}$)	H·$[CH_2]_n$·H (cm.$^{-1}$)	Polyesters of acid (cm.$^{-1}$)	n	Acid	(cm.$^{-1}$)	H·$[CH_2]_n$·H (cm.$^{-1}$)	Polyesters of acid (cm.$^{-1}$)
2	Succinic (β)	804	822	800—810	7	Azelaic	726	723	—
3	Glutaric (α)	754	748	—	8	Sebacic	722	722	720—725
4	Adipic	733	732	733—740	10	Dodecanedioic	723	720	—
5	Pimelic	731	728	—	14	Hexadecanedioic	727, 721	722	—
6	Suberic	725	726	—	16	Octadecanedioic	727, 720	—	—

The crystalline bands at 1300—1350 cm.$^{-1}$ are assigned to $\delta(CH_2)$ wag or twist (Sheppard and Simpson, *Quart. Rev.*, 1953, **7**, 1, 19) and are also dependent upon configuration. We assign the " crystalline " bands given in the Table to the out-of-plane $[CH_2]_n$ deformations of a methylene chain (Vallance-Jones and Sutherland, *Nature*, 1947, **160**, 567; Sheppard and Sutherland, *ibid.*, **159**, 739; Sheppard and Simpson, *loc. cit.*; Axford and Rank, *J. Chem. Phys.*, 1950, **18**, 51). Sheppard and Simpson (*loc. cit.*) discuss this assignment in detail and state that it only occurs in substantially *trans*-configurations. Where other discrete rotational isomers occur (Brown, Sheppard, and Simpson, *Discuss. Faraday Soc.*, 1950, **9**, 261) the corresponding vibration moves to higher frequencies. Calculations (Person and Pimental, *J. Amer. Chem. Soc.*, 1953, **75**, 532) of the dependence of the frequency of this vibration upon the phase angle of the chain confirm that this assignment relates to the zig-zag *trans*-configuration of the $[CH_2]_n$ chain.

Good agreement is observed (see Table) between the frequencies of $\delta[CH_2]_n$ rocking for dicarboxylic acids and the corresponding *n*-paraffins. The virtual absence of this $\delta[CH_2]_n$ band in the molten dicarboxylic acids is therefore interpreted as meaning that no appreciable proportion of the molecules retain the *trans*-configuration. In some of the dicarboxylic acids, this might have been plausibly accounted for by cyclic association favouring other configurations, but as the same phenomenon is observed in their polyesters (Part I, *loc. cit.*) the explanation is not favoured. Instead, we put forward the hypothesis of a continuous and random configuration of the $[CH_2]_n$ chains. To distinguish this from the normal type of discrete rotational isomers we propose the term " non-discrete rotational isomerism " for this phenomenon.

During this investigation our attention was drawn to the work of Sinclair, McKay, and Jones (*J. Amer. Chem. Soc.*, 1952, **74**, 2570), who reported that the spectra of long-chain monocarboxylic acids show similar changes, being ill-defined in the amorphous state. Subsequently, Neuilly (*Compt. rend.*, 1954, **238**, 63) observed similar changes for somewhat shorter-chain acids. In the monocarboxylic acids, however, the effects are less marked in that neither the 720-cm.$^{-1}$ ($\delta[CH_2]_n$) nor the 930-cm.$^{-1}$ [δ(OH)] band actually disappears in the liquid state, although they become somewhat less intense.

Sinclair *et al.* and Neuilly put forward the explanation of rotational isomerism, but regard the liquids as containing a large number of discrete isomers, although separate bands are not observable for these. Since the acids examined by Sinclair *et al.* were from C_{14} to C_{21}, the number of discrete isomers would be so large as to make it impracticable to decide whether the rotational isomerism is discrete or non-discrete. However, the shorter dicarboxylic acids considered in this paper show no evidence of discrete rotational isomers in the liquid state, although in the corresponding *n*-paraffins these are clearly shown (Axford and Rank, *J. Chem. Phys.*, 1949, **17**, 430). We regard this as clear evidence for non-discrete rotational isomerism in the dicarboxylic acids.

In non-associating liquids, the only force tending to overcome the barrier to free rotation about the C–C bonds (*ca.* 3 kcal./mole; Pauling, " Nature of the Chemical Bond," Oxford, 1948, p. 90) is that arising from collisions involving van der Waals forces. This is normally only sufficient to rotate the molecule from one discrete rotational isomer to another. However, where strong intermolecular forces are involved [the energy of hydrogen-bonding in the acids is *ca.* 8 kcal./(CO_2H); Pauling, *op. cit.*, p. 307] the extra force is considered sufficient not only to rotate the bonds, but also to constrain them in any intermediate configuration. The molecules therefore adopt a continuous range of random configurations rather than a number of discrete rotational isomers.

The constraining effect of the terminal carboxyl groups should be somewhat less noticeable for longer-chain acids for which discrete rotational isomerism of the type proposed by Sinclair *et al.* (*loc. cit.*) may occur. Moreover, since $\delta[CH_2]_n$ rocking is asymptotic to 720 cm.$^{-1}$ in long-chain compounds, a considerable proportion of rotational isomers would contain *trans*-segments of $n \geqslant 6$ and thus show a 720-cm.$^{-1}$ band.

Polymorphism of Glutaric Acid.—It is well known (Kendall, *Analyt. Chem.*, 1953, **25**, 382) that polymorphic modifications show spectral differences. The polymorphs of glutaric acid show a shift of the $\delta[CH_2]_n$ band from 762 cm.$^{-1}$ for the β-form to 754 cm.$^{-1}$ for the metastable α-form (obtained from the melt). This implies (Person and Pimental, *loc. cit.*) that the β-form has the less planar configuration, and is in agreement with *X*-ray findings (Morrison and Robertson, *J.*, 1949, 1001), *i.e.*, that the $C_{(1)}$–$C_{(2)}$ bond is rotated 14°. No *X*-ray work on α-glutaric acid is known, but from the $\delta[CH_2]_n$ absorption we would expect that it would have a more planar configuration of the carbon chain.

We thank Dr. G. B. Barlow for preparing the octadecanedioic acid, and the Dunlop Rubber Company for permission to publish this work.

Chemical Research Division, Dunlop Research Centre, Birmingham, 24. [*Received, January 3rd*, 1955.]

ω-Halogenomethyl-pyridines, -quinolines, and -isoquinolines. Part V. Preparation of Compounds related to* 1 : 2-*Di-2′-quinolylethane.*

By D. Ll. Hammick, C. N. Lammiman, E. D. Morgan, and A. M. Roe.

[Reprint Order No. 6192.]

Dehalogenation of ω-halogenoquinaldines with copper in pyridine has given symmetrical diquinolyl-acetylene, -ethylene, -dibromoethylene, and -dichloroethylene. The ethylenes have been isomerized by irradiation, and in the case of diquinolylethylene, configurations have been assigned.

In continuation of our studies of ω-halogenomethyl quinolines, we have sought a convenient route to 1 : 2-di-2′-quinolylethane and related coumponds from the readily prepared ω-halogenoquinaldines. 1 : 2-Di-2′-quinolylethane was prepared by Brown, Hammick, and Thewlis (*J.*, 1951, 1145) by Würtz synthesis from ω-monobromoquinaldine. It was earlier obtained from the products of the action of sulphur on quinaldine by von Miller (*Ber.*, 1888, **21**, 1827), who called it " diquinaldyl " but did not establish its structure. Walker, Baldwin, Thayer, and Corson (*J. Org. Chem.*, 1951, **16**, 1805) repeated von Miller's work and identified the product as 1 : 2-di-2′-quinolylethane. This method is simple but wasteful; it has now been modified to give fair yields and is superior to the four-stage synthesis *via* ω-monobromoquinaldine with its very inefficient Würtz reaction.

Johnson, Smith, Stacey, and Tatlow (*J.*, 1952, 4710) report a reaction with copper in pyridine, of aromatic compounds having a trichloromethyl or dichloromethylene group, in which chlorine is eliminated to give substituted ethylenes and ethanes. We have successfully adapted this reaction to the preparation of 1 : 2-di-2′-quinolyl-acetylene and -ethylene, and of the 1 : 2-dihalogenated derivatives of the latter from ω-halogenoquinaldines.

* Part IV, *J.*, 1953, 1369.

ωωω-Tribromoquinaldine reacts exothermally with copper in pyridine to give 1 : 2-di-2′-quinolylacetylene. By controlling the conditions we have been able to isolate either the acetylene or β-1 : 2-dibromo-1 : 2-di-2′-quinolylethylene.* ωωω-Trichloroquinaldine will only yield β-1 : 2-dichloro-1 : 2-di-2′-quinolylethylene. Attempts to make 1 : 1 : 2 : 2-tetrabromo- and 1 : 1 : 2 : 2-tetrachloro-1 : 2-di-2′-quinolylethane have been unsuccessful.

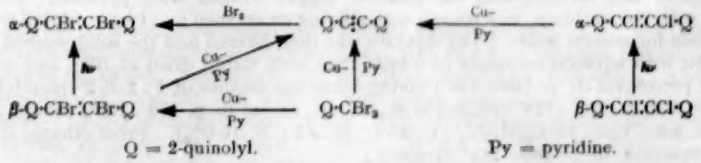
ωω-Dibromoquinaldine under similar treatment gives β-1 : 2-di-2′-quinolylethylene. Slow reaction at room temperature in an attempt to make 1 : 2-dibromo-1 : 2-di-2′-quinolylethane also gave β-1 : 2-di-2′-quinolylethylene. This compound (m. p. 189—190°) has been shown by mixed melting point and infrared spectrum to be identical with the compound made by the method of Walker *et al.* (*loc. cit.*). Attempts to obtain the compound reported by Kaplan and Lindwall (*J. Amer. Chem. Soc.*, 1943, **65**, 927) as 1 : 2-di-2′-quinolylethylene (m. p. 325°) were unsuccessful and gave either the ethylene melting at 190° or deoxyquinaldoin, m. p. 221°. Walker *et al.* (*loc. cit.*) reported the compound as yellow needles, but after careful purification the compound is colourless.

The reaction could not be extended to the preparation of 1 : 2-di-2′-quinolylethane because ω-monobromoquinaldine reacts with pyridine (or quinoline) with the rapid formation of quaternary salts (cf. Brown, Hammick, and Thewlis, *loc. cit.*). During this work a single-stage reduction of ωωω-tribromoquinaldine to ω-monobromoquinaldine (74%) in tetralin has been developed which is superior to previous preparations from the tribromo- or dibromo-quinaldine (cf. Brown and Hammick, *J.*, 1950, 628; Brown, Grice, Hammick, and Thewlis, *J.*, 1951, 1149). The Würtz synthesis of the ethane is not of preparative value; the compound may be obtained in fair yield by a modification of the procedure of Walker *et al.* (*loc. cit.*). When pure, the ethane is colourless.†

The β-unsaturated compounds are unusually resistant to bromine or chlorine under normal conditions. The dibromoethylene is very inert: it resists prolonged treatment with alcoholic silver nitrate, silver acetate in acetic acid, potassium permanganate in acetone, dilute or concentrated sulphuric acid, aqueous sodium hydroxide, and even fusion with potassium hydroxide. The infrared spectrum showed that the bromine was not attached to the quinolyl nuclei, and this was confirmed by treatment for eight hours with copper in pyridine, which gave the acetylene. Even 1 : 2-dibromo-1 : 2-di-2′-quinolylethane (made by the method of Walker *et al.*, *loc. cit.*) resists debromination with silver nitrate and acid and alkaline hydrolysis.

From the reaction of the acetylene with bromine, the only compound obtained analysed as dibromodiquinolylethylene, but it melted 80° higher, and its monopicrate decomposed 60° higher than that of β-dibromodiquinolylethylene. We have shown that this compound is an isomer of β-1 : 2-dibromo-1 : 2-di-2′-quinolylethylene. Irradiation of β-dibromodiquinolylethylene with ultraviolet light converted it into the higher-melting isomer. Similarly, ultraviolet irradiation of β-dichlorodiquinolylethylene and β-diquinolylethylene produced higher-melting, less soluble isomers. We distinguish these new forms of the ethylenic compounds by the prefix α, and the lower-melting, more soluble forms by the prefix β.

In order to confirm the structure of α-1 : 2-dichloro-1 : 2-di-2′-quinolylethylene, it was converted into 1 : 2-di-2′-quinolylacetylene, which was isolated after one hour's treatment



with copper in boiling pyridine. The β-dichlorodiquinolylethylene, after five hours under similar conditions, was recovered unchanged.

* For significance of *β-*, see below.

† *Added, June 3rd*, 1955.—Mr. J. A. Veitch, in this laboratory, has succeeded in preparing this compound from quinaldinyl-lithium in better yield.

When *cis-trans*-isomers of a substance exist, generally one of the isomers will approach more closely to coplanarity (the position of maximum elongation) than the other, and will therefore exhibit greater resonance; the optical absorption of the two isomers will therefore differ, that of the elongated isomer being the more intense (Mulliken, *J. Chem. Phys.*, 1939, **7**, 364).

Molecular models of 1 : 2-di-2′-quinolylethylene show that the *trans*-isomer can assume a planar configuration, whereas in the *cis*-form the molecule can never be planar because the quinolyl rings overlap. Thus we would predict that the *trans*-form, having the longer conjugated path, would absorb more intensely in the ultraviolet region. The spectrum of the β-ethylene bears a strong resemblance to that of 2 : 2′-dinaphthyl which can assume a completely conjugated planar structure. The α-ethylene has an absorption spectrum similar to that of quinoline itself but with twice the intensity, indicating loss of conjugation between the quinolyl rings. This is parallel to the case of the considerably sterically hindered 1 : 1′-dinaphthyl which has an absorption similar to that of naphthalene (Friedel, Orchin, and Reggel, *J. Amer. Chem. Soc.*, 1948, **70**, 199) (see Table).

Compound *	$\lambda_{max.}$	ϵ	$\lambda_{max.}$	ϵ	$\lambda_{max.}$	ϵ
β-Di-Q-ethylene	2725	49,500	—	—	3500	36,000
2 : 2′-Dinaphthyl †	2550	89,000	—	—	3100	18,000
α-Di-Q-ethylene	2350	30,000	2700	10,000	3130 ¶	12,500
1 : 1′-Dinaphthyl †	2300	39,000	—	—	2900 ¶	12,600
Quinoline ‡	—	—	2750	4,500	3110 ¶	6,300
α-Di-Cl-di-Q-ethylene	2350	31,500	—	—	3150 ¶	8,000
β-Di-Cl-di-Q-ethylene	2300	49,000	—	—	3200 ¶	12,800
α-Di-Br-di-Q-ethylene	2400	35,000	—	—	3150 ¶	8,000
β-Di-Br-di-Q-ethylene	2400	46,500	—	—	3200 ¶	13,300

* Q = 2-quinolyl. † Friedel, Orchin, and Reggel, *loc. cit.* ‡ Morton and de Gouveia, *J.*, 1934, 916; Sutherland and Compton, *J. Org. Chem.*, 1952, **17**, 1257. ¶ Approximate centre of fine-structure bands.

The infrared spectra support the evidence that α-1 : 2-di-2′-quinolylethylene is the *cis*-isomer, and the β-compound is *trans*.

The steric effect of the halogen atoms in the halogenoethylenes prevents *both cis-* and *trans*-isomers being completely planar, and hence all their ultraviolet spectra are different from that of β-1 : 2-di-2′-quinolylethylene; hence the spectral evidence cannot be used to determine the configuration of the halogenated ethylenes.

We note that 1 : 2-di-(6-methyl-2-quinolyl)ethylene-1 : 2-diol has been formulated as a hydrogen-bonded, completely conjugated, *trans*-structure (Buehler and Edwards, *J. Amer. Chem. Soc.*, 1952, **74**, 977); but it now appears that this is not supported by the ultraviolet spectrum which resembles that of quinoline and of our non-conjugated diquinolylethylenes.

Experimental

1 : 2-*Di*-2′-*quinolylacetylene*.—ωωω-Tribromoquinaldine (Hammick, *J.*, 1923, **123**, 2882) (20 g.) was dissolved in purified pyridine (125 ml.), and copper bronze powder (15 g.) added. Commercial copper bronze powder was used, freshly prepared copper powder as used by Johnson *et al.* (*loc. cit.*) showing no advantages. The mixture was refluxed for 3 hr., then cooled slightly and filtered, and the residual copper washed with pyridine. The filtrate, combined with the washings, was poured with stirring on crushed ice (1 kg.), diluted with water, and set aside for several hours. The mixture was then filtered and the solid washed free from copper salts with aqueous ammonia (*d* 0·880), then with water, dried at 100°, and crystallized from light petroleum (b. p. 100—120°) giving colourless needles of 1 : 2-di-2′-quinolylacetylene (1·9 g., 25%), m. p. 176—178° (Walker *et al.*, *loc. cit.*, record m. p. 179—180°) (Found: C, 85·0; H, 4·8; N, 9·5. Calc. for $C_{20}H_{12}N_2$: C, 85·7; H, 4·3; N, 10·0%). From ethanol it forms an insoluble dipicrate, m. p. 286—288° (decomp.).

β-1 : 2-*Dibromo*-1 : 2-*di*-2′-*quinolylethylene*.—A mixture of copper bronze powder (10 g.) and purified pyridine (30 ml.) was placed in a 1-l. 3-necked flask fitted with a mechanical stirrer, a dropping funnel, and a calcium chloride tube. A solution of ωωω-tribromoquinaldine (20 g.) in pyridine (100 ml.) was added dropwise during 1 hr. at room temperature. The solution was stirred for a further 2 hr., then filtered and washed as in the previous experiment and poured on ice. The insoluble material was filtered off and washed as before. Crystallization from

light petroleum gave β-1 : 2-*dibromo*-1 : 2-*di*-2′-*quinolylethylene* (4 g., 36%) as pale yellow needles, m. p. 141—142° (Found : C, 54·4; H, 3·0; N, 6·4; Br, 36·2. $C_{30}H_{18}N_2Br_2$ requires C, 54·5; H, 2·7; N, 6·4; Br, 36·4%). The *monopicrate* crystallized from methanol as yellow plates, m. p. 188—189° (Found : C, 46·8; H, 2·5; N, 9·8; Br, 23·4. $C_{36}H_{19}O_7N_5Br_2$ requires C, 46·7; H, 2·2; N, 10·5; Br, 23·9%). The *dihydrobromide*, m. p. 260—263° (decomp.), crystallizes from acetone (Found : C, 40·1; H, 2·3; N, 4·9; Br, 53·0. $C_{30}H_{14}N_2Br_4$ requires C, 39·9; H, 2·3; N, 4·7; Br, 53·2%).

The dibromoethylene is recovered substantially unchanged after 25 hr. in concentrated sulphuric acid at 145°, or after fusion with potassium hydroxide for 2½ min.

FIG. 1.

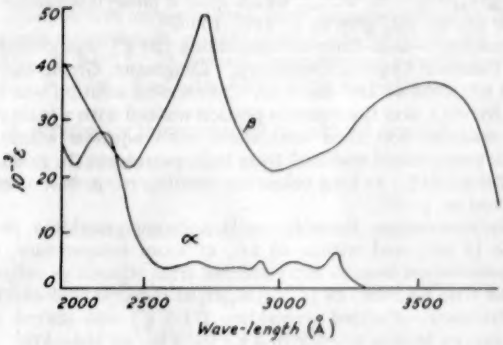
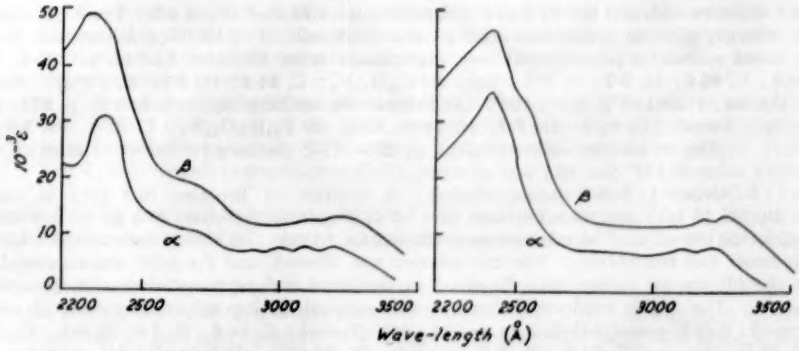


FIG. 2.

FIG. 3.



Absorption spectra of (FIG. 1) 1 : 2-*di*-2′-*quinolylethylene*, (FIG. 2) 1 : 2-*dichloro*-1 : 2-*di*-2′-*quinolylethylene, and* (FIG. 3) 1 : 2-*dibromo*-1 : 2-*di*-2′-*quinolylethylene*.

β-1 : 2-*Dichloro*-1 : 2-*di*-2′-*quinolylethylene*.—Copper bronze powder (2 g.) was added to a solution of ωωω-trichloroquinaldine (Hammick, *loc. cit.*) (2 g.) in pyridine (30 ml.), and the mixture refluxed for 15 min., then filtered and the filtrate poured on crushed ice. The material which separated was collected and washed with water and aqueous ammonia (*d* 0·880). β-1 : 2-*Dichloro*-1 : 2-*di*-2′-*quinolylethylene* (0·3 g., 22%) crystallized from light petroleum as colourless prisms, m. p. 94—95° (Found : C, 68·1; H, 3·5; N, 8·1; Cl, 20·5. $C_{30}H_{18}N_2Cl_2$ requires C, 68·4; H, 3·4; N, 8·0; Cl, 20·2%). The *monopicrate* crystallized from ethanol as yellow needles, m. p. 184—185° (Found : C, 54·1; H, 2·9; N, 12·6; Cl, 12·5. $C_{36}H_{19}O_7N_5Cl_2$ requires C, 53·8; H, 2·6; N, 12·1; Cl, 12·5%).

Debromination of β-1 : 2-*Dibromo*-1 : 2-*di*-2′-*quinolylethylene*.—β-Dibromodiquinolylethylene (0·7 g.) was dissolved in purified pyridine (25 ml.), and copper bronze powder (1 g.) added. This mixture was refluxed for 8 hr., filtered and poured on crushed ice. After the usual washing,

the dark brown solid was recrystallized several times from methanol. It was identified as 1 : 2-di-2′-quinolylacetylene (0·07 g., 15%), m. p. 175—177° (mixed m. p. 175—176°) (Found : C, 84·9; H, 4·7; N, 10·7. Calc. for $C_{30}H_{18}N_2$: C, 85·7; H, 4·3; N, 10·0%).

β-1 : 2-*Di-2′-quinolylethylene.*—Copper bronze powder (6 g.) was heated with ωω-dibromoquinaldine (Sharp, *J. Pharm. Pharmacol.*, 1949, **1**, 395) (10 g.) in purified pyridine (100 ml.) for 30 min. The product was isolated as in the previous experiments, and after drying at 100° crystallized from light petroleum as colourless crystals of β-1 : 2-di-2′-quinolylethylene (0·85 g., 18%), m. p. 189—190° (no depression on admixture with a sample made by the method of Walker *et al.*, *loc. cit.*) (Found : C, 84·9; H, 5·0; N, 9·1. Calc. for $C_{20}H_{14}N_2$: C, 85·1; H, 5·0; N, 9·9%). It forms an insoluble dipicrate from ethanol, m. p. 286—288° (decomp.).

Kaplan and Lindwall's method (*loc. cit.*) gave only deoxyquinaldoin, m. p. 221° (Found : N, 9·4. Calc. for $C_{20}H_{14}ON_2$: N, 9·5%), which gave a phenylhydrazone from ethanol, m. p. 148—149° (Walker *et al.*, *loc. cit.*, give m. p. 149—150·5°).

ω-*Monobromoquinaldine.*—ωωω-Tribromoquinaldine (30 g.) was stirred in purified tetralin (480 ml.; Vogel, " Practical Organic Chemistry," Longmans, Green and Co., London, 1948, p. 825) at 100° for 6 hr., then at 150° for 2 hr. The cooled solution was extracted with dilute sulphuric acid (25% by vol.), and the aqueous portion washed with a little chloroform to remove tetralin. The acid solution was then neutralized with aqueous ammonia, in an ice-bath. Crystallization of the precipitated material from light petroleum (b. p. 60—80°) gave ω-monobromoquinaldine (12·9 g., 74%) as long colourless needles, m. p. 57°. Brown, Hammick, and Thewlis (*loc. cit.*) record m. p. 57°.

N-2-*Quinolylmethylquinolinium Bromide.*—ω-Monobromoquinaldine (0·5 g.) was dissolved in purified quinoline (7 ml.) and within 48 hr., at room temperature, solid was deposited. N-2-*Quinolylmethylquinolinium bromide* recrystallized from ethanol as yellow plates, m. p. 222—223° (Found : C, 64·3; H, 4·3; Br, 22·7. $C_{19}H_{15}N_2Br$ requires C, 6·49; H, 4·3; Br, 22·8%).

1 : 2-*Di-2′-quinolylethane.*—Purified quinaldine (71·5 g.) was stirred under nitrogen with sulphur (16 g.) and copper bronze powder (0·5 g.) for 9 hr. at 165—170°. The temperature is critical for optimum yield. The cold solution was poured into 6N-sulphuric acid (200 ml.) and aqueous sodium hydroxide (10%) added to the filtered solution. The tar deposited below pH 4·0 was removed, and the 1 : 2-di-2′-quinolylethane collected at pH 4·5. From the residue, made strongly alkaline, quinaldine (42·3 g.) was recovered. 1 : 2-Di-2′-quinolylethane (5·8 g., 20% based on unrecovered quinaldine), crystallized from benzene, had m. p. 162·5—163° (Found : C, 84·6; H, 5·7; N, 9·9. Calc. for $C_{20}H_{16}N_2$: C, 84·3; H, 5·7; N, 9·9%). Walker *et al.* (*loc. cit.*) record m. p. 164—165°. The extremely insoluble dipicrate had m. p. 273—275° (decomp.) (Found : C, 52·2; H, 3·0; N, 15·1. Calc. for $C_{32}H_{22}O_{14}N_8$: C, 51·8; H, 3·0; N, 15·1%). Walker *et al.* (*loc. cit.*) record m. p. 275—280° (decomp.); Brown, Hammick, and Thewlis's value of 177° (*loc. cit.*) was an error.

α-1 : 2-*Dibromo*-1 : 2-*di-2′-quinolylethylene.*—A solution of bromine (0·5 ml.) in carbon tetrachloride (5 ml.) was added to one of 1 : 2-di-2′-quinolylacetylene (0·5 g.) in dry carbon tetrachloride (50 ml.). The mixture was refluxed for 10 min., by which time all the solid first precipitated had redissolved. The hot solution was filtered, and the solid which crystallized from the filtrate on cooling was dissolved in methanol and reprecipitated with 2N-aqueous ammonia. The white solid crystallized from methanol, giving colourless prisms of α-1 : 2-*dibromo*-1 : 2-*di-2′-quinolylethylene*, m. p. 222—223° (Found : C, 54·6; H, 3·0; N, 6·4; Br, 36·3. $C_{20}H_{12}N_2Br_2$ requires C, 54·5; H, 2·7; N, 6·4; Br, 36·4%). It formed a *monopicrate* which crystallized from ethanol as yellow needles, m. p. 238—239° (decomp.) (Found : C, 46·9; H, 2·3; N, 10·7; Br, 23·9. $C_{26}H_{15}O_7N_5Br_2$ requires C, 46·7; H, 2·2; N, 10·5; Br, 23·9%).

Irradiation of β-1 : 2-*Dibromo*-1 : 2-*di-2′-quinolylethylene.*—A solution of β-1 : 2-dibromo-1 : 2-di-2′-quinolylethylene (1 g.) in dry methanol (50 ml.) was irradiated with ultraviolet light from an 80-w mercury-vapour lamp for 5 days, by which time a deposit of crystals had formed in the container (a thin-walled soda-glass test-tube). The crystals were collected and recrystallized from methanol as colourless needles, m. p. 220—221°. There was no depression of the melting point when this substance was mixed with α-1 : 2-dibromo-1 : 2-di-2′-quinolylethylene prepared as above. The product formed a monopicrate, yellow needles (from ethanol), m. p. and mixed m. p. 240—241° (decomp.).

Irradiation of β-1 : 2-*Dichloro*-1 : 2-*di-2′-quinolylethylene.*—β-1 : 2-Dichloro-1 : 2-di-2′-quinolylethylene (1 g.) in dry methanol (200 ml.) was irradiated as for β-1 : 2-dibromo-1 : 2-di-2′-quinolylethylene. α-1 : 2-*Dichloro*-1 : 2-*di-2′-quinolylethylene* recrystallized from methanol as colourless needles, m. p. 172—173°, depressed to 90° on admixture with the β-form. A *monopicrate* crystallized from methanol as yellow needles, m. p. 222—224° (decomp.) (Found :

C, 53·4; H, 2·9; N, 12·3; Cl, 12·2. $C_{28}H_{15}O_7N_3Cl_2$ requires C, 53·8; H, 2·6; N, 12·1; Cl, 12·5%).

Dechlorination of α-1 : 2-*Dichloro*-1 : 2-*di*-2′-*quinolylethylene*.—α-1 : 2-Dichloro-1 : 2-di-2′-quinolylethylene (0·45 g.) was refluxed in purified pyridine (2·5 ml.) with copper bronze powder for 1 hr. and, after cooling, poured on crushed ice. After isolation in the usual way, 1 : 2-di-2′-quinolylacetylene recrystallized from light petroleum as pale brown needles, m. p. and mixed m. p. 177—178°.

Irradiation of β-1 : 2-*Di*-2′-*quinolylethylene*.—The α-isomer is comparatively soluble in methanol, so the irradiation was carried out on a saturated solution of β-1 : 2-di-2′-quinolylethylene in methanol over an excess of the same compound. After several days' irradiation with ultraviolet light, crystals had been formed on the walls of the tube, and the original solid had dissolved. The product was recrystallized from benzene–methanol to give α-1 : 2-*di*-2′-*quinolylethylene* as colourless needles, m. p. 245° (Found : C, 85·0; H, 5·1; N, 9·95. $C_{20}H_{14}N_2$ requires C, 85·1; H, 5·0; N, 9·9%). It formed a comparatively unstable *dipicrate*, m. p. 147—151° (decomp.) (Found : N, 15·0. $C_{32}H_{20}O_{14}N_8$ requires N, 15·1%).

We thank Dr. F. B. Strauss for interpretation of infrared spectra.

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The Polysaccharides of Colocasia antiquorum (*Taro or Colocass*).

By El S. Amin.

[Reprint Order No. 5946.]

The starch of *Colocasia* tubers contains 28% of amylose. Periodate oxidation, and methylation and hydrolysis, indicate a chain length of 490 glucose units for amylose and 22 units for amylopectin. These results are similar to those for potato starch.

Colocasia mucilage yields D-galactose (88%), L-arabinose (8%), and uronic acid (2%). Hydrolysis of the main methylated fraction gave 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose (10%), 2 : 3 : 6-tri-*O*-methyl-D-galactose (87%), and 2 : 4-di-*O*-methyl-D-galactose (2·5%).

Colocasia (family Araceae) is widely cultivated and used as common food in Egypt. Its polysaccharides can be roughly distinguished as a water-soluble mucilage and insoluble starch granules.

The starch was isolated from the tubers after complete removal of the mucilage; its blue value corresponded to an average amylose content of 28·0%. It was then separated into amylose (30%) and amylopectin. Oxidation with periodate suggested a chain length of about 490 glucose units for amylose and 22 units per end-group for amylopectin. The latter value was found to be in agreement with the result obtained by hydrolysis of methylated amylopectin. Examination of the fission products of the methylated amylose and amylopectin on a paper chromatogram showed mainly 2 : 3 : 6-tri-*O*-methylglucose and a little 2 : 3-di-*O*-methylglucose. 2 : 3 : 4 : 6-Tetra-*O*-methylglucose was found only in the hydrolysate of methylated amylopectin, suggesting a chain length of not less than 100 units for amylose and 22 units for amylopectin (Hough, Jones, and Wadman, *J.*, 1952, 3393). The dimethylglucose may have arisen from incomplete methylation or from demethylation during hydrolysis (Hirst, Hough, and Jones, *J.*, 1949, 928; Barker, Bourne, and Wilkinson, *J.*, 1950, 3027). Confirmation of the above results was obtained by the isolation of crystalline glucosazone, 2 : 3 : 4 : 6-tetra-*O*-methyl-*N*-phenyl-D-glucosylamine, 2 : 3 : 6-tri-*O*-methyl-D-glucose, and syrupy 2 : 3-di-*O*-methyl-D-glucose.

Colocasia mucilage was extracted from the tubers with water at room temperature and purified by several reprecipitations from alcohol and formation of a water-insoluble copper complex. It had a low positive optical rotation and exhibited a slight reducing action on

Fehling's solution. Attempts to separate the pentose and uronic acid by fractional precipitation were unsuccessful. Hydrolysis of the mucilage by mineral acid and paper chromatography gave galactose (88%) and arabinose (8%), identification being as D-galactose methylphenylhydrazone, mucic acid, and L-arabinose α-benzoylphenylhydrazone. The uronic acid content was 2%. The occurrence of D-galactose and L-arabinose is common in a wide variety of plant materials. Further information concerning the mode of linkage of the various components in *Colocasia* mucilage was obtained by methylation of the acetyl derivative with methyl sulphate and sodium hydroxide, followed by methyl iodide and silver oxide and fractionation. The low negative specific rotation of the main fraction indicates that the sugar units are joined by β-linkages. Hydrolysis and examination of the fission products on the paper chromatogram showed 2 : 3 : 4 : 6-tetra-*O*-methylgalactose (10%), 2 : 3 : 6-tri-*O*-methylgalactose (87%), and 2 : 4-di-*O*-methylgalactose (2·5%). This suggests that the main linkage in the polysaccharide is through carbon atoms 1 and 4. Hydrolysis of the second fraction gave 2 : 3 : 5-tri-*O*-methylarabinose (19%), besides the above-mentioned methyl-sugars. In confirmation, crystalline 2 : 3 : 4 : 6-tetra-*O*-methyl-*N*-phenyl-D-galactosylamine, 2 : 3 : 6-tri-*O*-methyl-D-galactonolactone, 2 : 3 : 5-tri-*O*-methyl-L-arabonolactone, and 2 : 3 : 5-tri-*O*-methyl-L-arabonamide were prepared, as well as syrupy 2 : 4-di-*O*-methyl-D-galactose.

Experimental

Chromatography was carried out on Whatman No. 1 filter paper sheets by the descending method (Partridge, *Biochem. J.*, 1948, **42**, 238), *n*-butanol–ethanol–water (5 : 1 : 4 v/v) being used. Sugars and methyl-sugars were detected with *p*-anisidine hydrochloride as spray reagent. Specific rotations and viscosity determinations were carried out at 28°. Evaporations were done under reduced pressure at 50° unless otherwise stated. The results were calculated on an ash-free basis and on an actual starch content. Treatments with alkali were done in nitrogen atmosphere.

Preparation of Colocasia *Starch.*—*Colocasia* tubers (10 kg.) were freshly harvested in February, 1953 (Alexandria, Egypt). The average weight of each tuber was ½ kg. The tubers were washed thoroughly, the outer fibrous material was removed, and the flesh cut into thin slices and soaked in water (20 l.) containing sulphur dioxide for a week. The starch was isolated according to directions of Hirst, Jones, and Roudier (*J.*, 1948, 1779). The fatty acids were removed by Schoch's method (*J. Amer. Chem. Soc.*, 1942, **64**, 2954), and the product was dried at room temperature and pressure (yield 200 g., 2%). The yield was not quantitative as much of the original starch remained enclosed in the unruptured cells.

Properties of Colocasia *Starch.*—Microscopic examination revealed traces of fibrous material admixed with the granules (size 3—10 μ). The blue value was 0·47 (procedure of Wilson, Schoch, and Hudson, *ibid.*, 1943, **65**, 1380). Based on a blue value of 1·64 for amylose and 0·01 for amylopectin, this suggests an amylose content of 28% (Found : H_2O, 14%; sulphated ash, 0·3%; N, 0·05%). $[\alpha]_D$ was +160° (*c*, 0·5 in 4% NaOH). The presence of anthocyanins was indicated according to the procedure of Campbell, Frahn, Hirst, Packman, and Percival (*J.*, 1951, 3489) : the pink colour changed to green on addition of a slight excess of sodium hydroxide solution. The gelation point was 70—75°, above which the starch formed a pale buff paste. The granules dispersed with difficulty in N-sodium hydroxide to give a pale brown solution.

According to a report by Prof. Dr. M. S. Ridi, Kasr El Aini, Faculty of Medicine, Cairo, the composition of *Colocasia* and potato tubers was as tabulated for duplicate analyses.

	Colocasia		Potato			*Colocasia*		Potato	
Water (%)	70·2,	74·0	76·2,	69·6	Fibre (%)	0·69,	—	—	1·4
Protein (%)	1·9,	2·0	1·9,	0·35	Ash (%)	1·6,	0·8	1·1,	0·53
Fat (%)	0·15,	0·04	0·2,	0·2	Caloric value	89·9,	98·0	90·0,	113·6
Carbohydrate (%) ...	21·5,	21·8	20·1,	27·6					

If the percentage (86·0%) of edible matter is considered, the amount of carbohydrate and the calorific value of *Colocasia* exceed that of potato.

Hydrolysis of Colocasia *Starch.*—A portion (60 mg.) was hydrolysed according to the procedure of Hough, Jones, and Wadman (*loc. cit.*), giving a syrup (52 mg.). Examination on the paper chromatogram showed only glucose (R_G 0·09), $[\alpha]_D$ +54° (equil.; *c*, 0·5 in H_2O). It gave glucosazone, m. p. and mixed m. p. 205°. Quantitative determination (Flood, Hirst, and Jones, *J.*, 1948, 1679) accounted for 85% of starch.

Fractionation of Colocasia *Starch*.—This was done according to the procedure of Bourne, Donnison, Haworth, and Peat (*J.*, 1948, 1687), with 60 g. of defatted material. The amylose was then further purified by four reprecipitations with butanol (yield 18 g.).

Amylose. This was a pale brown amorphous substance. It dissolved with difficulty in sodium hydroxide solution, giving a pale brown opaque solution. It had $[\alpha]_D$ +150° (*c*, 0·4 in 4% NaOH) (Found: H_2O, 14%; sulphated ash, 0·4%; N, 0·06%).

The amylopectin was isolated from the mother-liquor after precipitation of amylose, by addition of ethanol (5 parts) (yield 38 g.). It was a white amorphous substance, dissolved in sodium hydroxide solution to a clear solution, and had $[\alpha]_D$ +152° (*c*, 0·9 in 4% NaOH), and H_2O 15%.

The viscosity was measured according to the procedure of Potter, Hassid, and Joslyn (*J. Amer. Chem. Soc.*, 1949, **71**, 4075), being 0·95 for amylose and 0·92 for amylopectin.

Chain Length of Colocasia *Amylose and Amylopectin*.—A series of five portions each of amylose and amylopectin (200 mg. each) were treated with sodium periodate (Potter and Hassid, *ibid.*, 1948, **70**, 3488). The amount of 0·01N-barium hydroxide (0·75 and 5·57 ml.) after 25 hr. was taken as the end-point: it gave 22 glucose units as an average number per end-group for amylopectin and 490 units for amylose.

Acetylation of Colocasia *Amylose and Amylopectin*.—Each polysaccharide (4 g.) was twice acetylated by Hirst, Jones, and Roudier's method (*loc. cit.*), giving white amorphous substances (yield, 80% and 82% respectively), $[\alpha]_D$ (amylose) +172° (*c*, 1 in $CHCl_3$), (amylopectin) +168° (*c*, 1 in $CHCl_3$).

Methylation of Colocasia *Amylose*.—A portion of acetylated derivative (2 g.) was stirred with acetone (50 c.c.) and methylated eight times with methyl sulphate and sodium hydroxide (Clinton, Ballou, and Percival, *J.*, 1952, 1054). The final product was fractionated by successive extractions with light petroleum (b. p. 60—80°)–chloroform in the proportions, 90 : 10, 85 : 15, and 80 : 20. The main product (1·3 g.), obtained from the middle solvent mixture, had $[\alpha]_D$ +210° (*c*, 0·5 in $CHCl_3$) (Found: OMe, 41. Calc. for $C_9H_{16}O_5$: OMe, 45·6%), $\eta_{sp.}$ 0·4 (*c*, 0·5 in *m*-cresol). The other two fractions had the same methoxyl content and viscosity as above.

Hydrolysis of Methylated Colocasia *Amylose*.—A portion (400 mg.) was hydrolysed according to the procedure of Hough, Jones, and Wadman (*loc. cit.*) to a syrup (340 mg.) which on the paper chromatogram showed spots corresponding to 2 : 3 : 6-tri- (R_G 0·83) and 2 : 3-di-*O*-methylglucose (R_G 0·57). Quantitative estimation of the methyl sugars (Hirst, Hough, and Jones, *loc. cit.*), a phosphate buffer being used (Chanda *et al.*, *J.*, 1950, 1289), gave 2 : 3 : 6-tri- (94%) and 2 : 3-di-*O*-methylglucose (3%), the first of which was isolated crystalline from the paper chromatogram {yield 70 mg.; m. p. and mixed m. p. 120—121°, $[\alpha]_D$ +69° (equil.; *c*, 2·0 in H_2O)}.

Methylation of Colocasia *Amylopectin*.—The acetylated substance (2 g.) was methylated eight times as above. Attempts to fractionate the product with light petroleum and chloroform, as above, gave a main product (1·6 g.) from the 85 : 15 mixture, having $[\alpha]_D$ +212° (*c*, 0·5 in $CHCl_3$), $\eta_{sp.}$ 0·3 (*c*, 0·5 in *m*-cresol) (Found: OMe 42·5%). The two other fractions had the same methoxyl content and viscosity.

Hydrolysis of Methylated Colocasia *Amylopectin*.—(*a*) A portion (350 mg.) was hydrolysed as above, giving a syrup (320 mg.) the components of which were separated on the paper chromatogram, giving spots of 2 : 3 : 4 : 6-tetra- (R_G 1·00), 2 : 3 : 6-tri- (R_G 0·83), and 2 : 3-di-*O*-methylglucose (R_G 0·57). The methyl-sugars were determined as above: 2 : 3 : 4 : 6-tetra- (4·5%), 2 : 3 : 6-tri- (89%), and 2 : 3-di-*O*-methylglucose (5%). Another portion of the hydrolysate (170 mg.) was fractionated on the paper chromatogram, and crystalline 2 : 3 : 6-tri-*O*-methyl-D-glucose (85 mg.) isolated, with m. p. and mixed m. p. 121°, $[\alpha]_D$ +70° (equil.; *c*, 2·0 in H_2O) (Found: OMe, 41·0. Calc. for $C_9H_{18}O_6$: OMe, 41·9%).

(*b*) Methylated amylopectin (0·7 g.) was heated in methanolic 2% hydrochloric acid (50 c.c.) under reflux for 7 hr. The fully methylated sugar (42 mg.) was isolated from the mixture by Brown and Jones's method (*J.*, 1947, 1344). It was hydrolysed in N-sulphuric acid for 6 hr. to syrupy 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose (29 mg.), $[\alpha]_D$ +82° (*c*, 1 in H_2O) (Found: OMe, 52·0. Calc.: OMe, 52·5%). It gave an aniline derivative (8 mg.), m. p. and mixed m. p. 132° by the method of Hough, Jones, and Wadman (*loc. cit.*).

Colocasia *Mucilage*.—Tubers (12 kg.) were cleaned thoroughly, the fibrous outer skin was removed, and the flesh cut into thin slices. After 24 hours' soaking in N-hydrochloric acid (18 l.) the mucilage was dispersed in the aqueous solution. It was filtered through a sieve (50-cm. diameter, mesh 2 mm.). Extraction was repeated and the slices were then discarded. The whole extract was shaken with charcoal for 4 hr. at room temperature, then twice centrifuged

(3500, then 24,000 r.p.m.). The clear centrifugate was poured into 96% ethyl alcohol (5 parts) with stirring, giving a snow-white fibrous material. To reduce the high ash content (4·6%) the amorphous product was redispersed in water, 5% hydrochloric acid was added to a final normality of N, and the mucilage dialysed for 24 hr. (yield 360 g., 3%). The substance was further purified by dissolution in N-sodium hydroxide, acidification with acetic acid, centrifugation, and precipitation with alcohol. A portion (50 g.) was suspended in water (2·5 l.) and ammonia (*ca.* 2N) was added, with shaking, until the solution was neutral. A little undissolved material was removed on the centrifuge. A 10% solution of copper chloride (1 l.) was added dropwise and the resultant insoluble complex was removed on the centrifuge, and washed with water and alcohol, followed by ethanolic hydrogen chloride (5%) until the washings were copper-free and finally with ethanol until chloride-free. The product was dried to constant wt. in a vacuum at 50° (yield 42 g.). The mother-liquor after precipitation of the copper complex was concentrated to 100 c.c. and treated with alcohol (5 parts). The precipitate was treated as above, giving amorphous white material (1·5 g.), proved to be a polysaccharide.

Properties of Colocasia *Mucilage*.—It was a white amorphous substance insoluble in organic solvents, dissolved with difficulty in water but easily in alkali, had little reducing action on Fehling's reagent, was unaffected by saliva during 10 min. (Found: sulphated ash, 0·2; N, 0·05%), had $[\alpha]_D$ +13·4° (*c*, 0·6 in N-NaOH), $\eta_{sp.}$ 0·2 (c, 0·1 in N-NaOH), and gave 2% of uronic acid according to Lefèvre and Tollens's method (*Ber.*, 1907, **40**, 4513).

Acid Hydrolysis of Colocasia *Mucilage*.—A portion (650 mg.) was heated with N-sulphuric acid (5 c.c.) at 100° in a sealed tube for 12 hr. Flocculent material (15 mg.) was filtered off, and the filtrate neutralised with barium carbonate, de-ionised with a mixture of Amberlite resins IR-120 and IR-400 and concentrated to a syrup (580 mg.). Examination of the hydrolysate on the paper chromatogram showed spots of galactose (R_G 0·07) and arabinose (R_G 0·12). Quantitative determination of these sugars (Flood, Hirst, and Jones, *loc. cit.*) indicated galactose 88% and arabinose 8% (calc. as $C_6H_{10}O_5$ and $C_5H_8O_4$ respectively). Another portion of the hydrolysate (140 mg.) was fractionated on the paper chromatogram and the fractions were extracted with methyl alcohol. The first fraction had $[\alpha]_D$ +82° (equil.; *c*, 0·5 in H_2O), and gave D-galactose methylphenylhydrazone, m. p. and mixed m. p. 185° (decomp.) (Hirst, Jones, and Woods, *J.*, 1947, 1048), and mucic acid, m. p. and mixed m. p. 215° (Heyne and Whistler, *J. Amer. Chem. Soc.*, 1948, **70**, 2249). The second fraction had $[\alpha]_D$ +105° (equil.; *c*, 0·5 in H_2O), and gave L-arabinose α-benzoylphenylhydrazone (8 mg.), m. p. and mixed m. p. 170—171° (Hirst, Jones, and Woods, *loc. cit.*).

Acetylation of Colocasia *Mucilage*.—A portion (4·3 g.) of the dry powdered polysaccharide was warmed with pyridine (100 c.c.) for 2 hr. at 70°, then cooled and kept overnight at room temperature. Acetic anhydride (40 c.c.) was added dropwise during 1 hr. The mixture was incubated at 52° for 3 days. The solution was diluted with glacial acetic acid (100 c.c.) and poured into ethyl alcohol (2 l.; 96%) with stirring. The white amorphous product was isolated at the centrifuge, washed with alcohol and ether, and dried (yield 3·5 g.). Acetylation was repeated as above, giving a product (2·9 g.) of $[\alpha]_D$ +35° (*c*, 1 in $CHCl_3$).

Methylation of Colocasia *Mucilage*.—The acetylated material (2·8 g.) was stirred with acetone (150 c.c.) and methylated with methyl sulphate (70 c.c.) and 30% sodium hydroxide solution (140 c.c.) at 10° during 8 hr. Stirring was continued overnight at room temperature, and the reaction was completed by heating at 50° for ½ hr. After eight methylations, the product was purified by precipitation from light petroleum (b. p. 40—60°), giving a white amorphous substance (1·9 g.). It was remethylated twice with methyl iodide and silver oxide, giving a product (1·8 g.) of $[\alpha]_D$ −15° (*c*, 1 in acetone) (Found: OMe, 42%), $\eta_{sp.}$ 0·3 (*c*, 1 in $CHCl_3$). An attempt to fractionate the methyl derivative with light petroleum (b. p. 40—60°)–chloroform in the ratios 95 : 5, 90 : 10, and 85 : 15 gave mainly two fractions. The fraction (1·2 g.) from the last solvent mixture (85 : 15) had $[\alpha]_D$ −13° and gave furfuraldehyde 1·2%. The middle fraction (0·6 g.) had $[\alpha]_D$ −15° and gave furfuraldehyde 14·5%. The first fraction (600 mg.) was heated with methanolic hydrogen chloride (3%) in a sealed tube for 7 hr. at 100°. The product was neutralised with cold ethereal diazomethane, concentrated at room temperature, and refluxed with 4% hydrochloric acid for 7 hr., then neutralised with silver carbonate, filtered, de-ionised with a mixture of Amberlite resins IR-120 and IR-400, and evaporated to a syrup (450 mg.). Examination on the paper chromatogram showed spots of 2 : 3 : 4 : 6 tetra- (R_G 0·88), 2 : 3 : 6 tri- (R_G 0·71), and 2 : 4-di-*O*-methylgalactose (R_G 0·41). In a quantitative experiment the proportion of the methyl sugars was determined by the alkaline hypoiodite procedure of Hirst, Hough, and Jones (*loc. cit.*), giving 2 : 3 : 4 : 6-tetra- 10%, 2 : 3 : 6-tri- 87%, and di-*O*-methylgalactose 2·5%.

Another portion of the hydrolysate (160 mg.) was separated on the paper chromatogram, the methyl sugars were located, and sections of the different fractions extracted with hot methanol. The first fraction (Found : OMe, 50·5. Calc. for $C_{18}H_{20}O_6$: OMe, 52·5%) gave 2 : 3 : 4 : 6-tetra-*O*-methyl-*N*-phenyl-D-galactosylamine (12 mg.), m. p. and mixed m. p. 194° (Found : OMe, 38·9. Calc. for $C_{14}H_{25}O_5N$: OMe, 39·9%) (Hough and Jones, *J.*, 1950, 1199). The second fraction had $[\alpha]_D$ +88° (*c*, 1 in H_2O) (Found : OMe, 39·0. Calc. for $C_9H_{18}O_6$: OMe, 41·8%) and gave crystalline 2 : 3 : 6-tri-*O*-methyl-γ-D-galactonolactone (50 mg.), m. p. and mixed m. p. 98—99° (Hough and Jones, *loc. cit.*).

A portion (500 mg.) of the second methylated polysaccharide fraction was hydrolysed and the hydrolysate examined on the paper chromatogram as above. Spots of the above mentioned sugars were observed besides a spot of 2 : 3 : 5-tri-*O*-methylarabinose (R_G 0·64). That fraction was isolated from the paper chromatogram (95 mg.). It gave 2 : 3 : 5-tri-*O*-methyl-L-arabonolactone (30 mg.), m. p. and mixed m. p. 28°, and 2 : 3 : 5-tri-*O*-methyl-L-arabonamide (22 mg.), m. p. and mixed m. p. 134°, according to the procedure of Hirst, Jones, and Walder (*J.*, 1947, 1225).

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Studies in the Pyrolysis of Organic Bromides. Part IV. The Pyrolysis of sec.-Butyl Bromide.*

By ALLAN MACCOLL and P. J. THOMAS.

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sec.-Butyl bromide has been shown to decompose to butene and hydrobromic acid in the temperature range 300—350° homogeneously and according to a first-order law. The rate constant is expressible as $k_1 = 4{\cdot}27 \times 10^{12} \exp(-43{,}800/RT)$ (sec.$^{-1}$). Added propene and *cyclo*hexene do not radically alter the rate and it is concluded that the predominant process is the unimolecular elimination of hydrogen bromide.

IN Parts I—III,* three distinct mechanisms have been observed for the pyrolyses of organic bromides in the gaseous phase : allyl bromide decomposes by a radical non-chain process, *n*-propyl bromide by a radical-chain mechanism, and *iso*propyl bromide by direct unimolecular elimination of hydrogen bromide. The essential steps in the chain mechanism are :

$$RBr \longrightarrow R + Br \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$Br + RBr \longrightarrow R'Br + HBr \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$R'Br \longrightarrow M + Br \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

together with some chain-ending step (M represents an olefin). The case of allyl bromide is distinctive in that the allyl radical $CH_2\overset{\frown}{-}CH\overset{\frown}{-}CH_2$ is strongly stabilised by resonance, as is also true of the bromoallyl radical $CH_2\overset{\frown}{-}CH\overset{\frown}{-}CHBr$. The non-chain character of the pyrolysis can in the main be ascribed (i) to the weakness of the C–H bond in the CH_2Br group, so that attack by a bromine atom is directed to this group, and (ii) to the lack of facility of the chain-propagating step (3). The behaviour of the propyl bromides has been explained in terms of propagating (P) radicals and stopping (S) radicals, *viz.* :

$CH_3{\cdot}\dot{C}H{\cdot}CH_2Br$ (P) $\qquad$ $CH_3{\cdot}CHBr{\cdot}\dot{C}H_2$ (P)

$CH_3{\cdot}CH_2{\cdot}\dot{C}HBr$, $\dot{C}H_2{\cdot}CH_2{\cdot}CH_2Br$ (S) $\qquad$ $(CH_3)_2\dot{C}Br$ (S)

It has been shown in Part III that the atom attack on *n*-propyl bromide leads in the main to P radicals, whereas in *iso*propyl bromide it leads to S radicals. Further the P radicals

* Parts I—III, *J.*, 1955, 965, 973, 979.

from *n*-propyl bromide decompose very much more rapidly than those from *iso*propyl bromide. The observed case of chain propagation in *n*-propyl bromide and its absence in *iso*propyl bromide are thus explained.

The pyrolysis of *sec.*-butyl bromide poses two questions: First, what effect, on the rate of unimolecular elimination of hydrogen bromide, has the replacement of a C–H bond in which the C atom is primary by one in which it is secondary? Secondly, will the chain mechanism be favoured by the fact that the P radicals can be produced by an attack on the C–H bond of a secondary group? That the unimolecular mechanism might be preferred is indicated in the literature: ethyl bromide (Lessig, *J. Phys. Chem.*, 1932, **36**, 225; Vernon and Daniels, *J. Amer. Chem. Soc.*, 1933, **55**, 922; Fugassi and Daniels, *ibid.*, 1938, **60**, 771; Daniels and Veltman, *J. Chem. Phys.*, 1939, **7**, 756; Roof and Daniels, *J. Amer. Chem. Soc.*, 1940, **62**, 2912; Roof, *ibid.*, 1944, **66**, 358) and *n*-propyl bromide (Part II) decompose by a chain mechanism, at least in part in the former case, whereas *sec.*-propyl bromide (Part III) and *tert.*-butyl bromide * (Kistiakowsky and Stauffer, *J. Amer. Chem. Soc.*, 1937, **59**, 165) decompose by unimolecular elimination of hydrogen bromide. This suggests that the nature of the C–Br bond is the most cogent factor in determining the mode of decomposition.

Experimental

Two commerical samples of *sec.*-butyl bromide were fractionated through a metre column, the middle fractions of constant physical properties being retained. Secondly, the bromide was prepared by treatment of fractionated *sec.*-butyl alcohol with constant-boiling hydrobromic acid. All samples showed the same kinetic behaviour. The b. p. was 91·4°/760 mm. (cf. Timmermans, "Physical Constants of Pure Organic Compounds," Elsevier, Netherlands, 1950, reports 91·2°, 91·24°, 91·3°), n_D^{25} 1·4342 (cf. Heston *et al.*, *J. Amer. Chem. Soc.*, 1950, **72**, 2072, who report 1·4342).

By analogy with the pyrolysis of other saturated bromides it may be concluded that the overall reaction is:

$$C_4H_9Br \longrightarrow C_4H_8 + HBr \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

As in the previous studies, the kinetics of the reaction were measured by studying both the rate of pressure increase and the rate of production of hydrogen bromide. Table 1 illustrates the

Table 1.

Method	Decomposition (%)									
Pressure	30·6	43·2	46·1	57·2	59·0	66·0	70·0	82·6	83·2	89·3
Anal.	30·7	44·6	46·0	58·5	59·3	65·8	71·0	83·5	81·9	89·2

agreement between the two methods. After a run, the products were completely condensable in liquid air, so it may be concluded that equation (4) represents the course of the decomposition.

The reaction followed a first-order law up to about 50% decomposition (see Fig. 1). The subsequent decrease in rate is best interpreted, as for *iso*propyl bromide, in terms of an equilibrium between (4) and the reverse reaction. That the first-order law is obeyed over a wider range implies that the equilibrium lies further towards the right. The homogeneity of the reaction was tested in the usual manner by packing the reaction vessel with thin-walled glass tubing, so as to increase the surface : volume ratio by a factor of five. The results obtained at two temperatures are shown in Table 2.

Table 2.

	At 311°.				*At* 333°.						
p_0 (mm.)	342	325	280	267	350	335	276	254	227	206	187
10^4k_1 (sec.$^{-1}$)	1·66	1·68	1·70	1·72	6·95	7·02	6·78	7·02	7·12	7·02	6·95

The mean values $1{\cdot}69 \times 10^{-4}$ and $7{\cdot}00 \times 10^{-4}$ sec.$^{-1}$, compared with the values for the unpacked vessel, $1{\cdot}70 \times 10^{-4}$ and $6{\cdot}61 \times 10^{-4}$ sec.$^{-1}$ (interpolated from the Arrhenius equation), show that the five-fold increase in the surface : volume ratio had little effect on the rate.

* The pyrolysis of *tert.*-butyl bromide has been re-investigated by G. D. Harden (Part VI), who has unambiguously demonstrated unimolecular elimination.

The variation of the reaction rate with temperature, in the range 300—350°, is set out in Table 3. The experimental results were fitted to the equation

$$k_1 = 4{\cdot}27 \times 10^{12} \exp(-43{,}800/RT)$$

the agreement between the observed and calculated values being excellent. The Arrhenius plot is shown in Fig. 2.

In order to test the pressure dependence of the rate constants over a wide pressure range, a number of runs were carried out at 333° (see Table 4) : there was no effect on the rate. The

FIG. 1. *The first-order plot, showing a departure from linearity after about 50% reaction.*

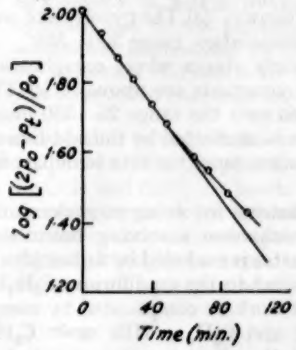
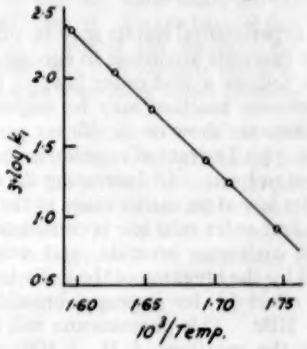


FIG. 2. *The Arrhenius plot.*



value at high pressures is slightly greater than that ($6{\cdot}70 \times 10^{-4}$ sec.$^{-1}$) obtained from the Arrhenius plot, perhaps because these experiments were performed in a rebuilt apparatus employing a vapour reservoir.

TABLE 3.

Temp.	299·5°	311·5°	317°	331·5°	341·5°	353°
No. of runs	7	7	7	6	3	4
10^4k_1 (sec.$^{-1}$)	0·717	1·71	2·49	5·98	10·8	21·9

TABLE 4. *Effect of pressure, at* 333°.

p_0 (mm.)	343	327	308	230	215	164	118	114	84
10^4k_1 (sec.$^{-1}$)	7·02	6·78	6·78	7·16	7·06	6·78	7·58	7·46	7·01
p_0 (mm.)	67	66·5	52	48·5	43	36·5	31	25	25
10^4k_1 (sec.$^{-1}$)	6·80	7·04	7·31	7·60	7·22	7·00	7·50	7·16	7·21

In order to test for the presence of bromine-atom chains, the decomposition was carried out in the presence of propene and *cyclo*hexene. The latter should be a particularly efficient inhibitor because of the C–H bond, in which the C is primary and adjacent to the double bond. Attack by a bromine atom would be facilitated both by this and by the resonance stabilisation of the *cyclo*hexenyl radical (cf. allyl). That *cyclo*hexene is in fact a powerful inhibitor has been shown in the case of *n*-propyl bromide. (The relative efficiencies of different inhibitors are under investigation and will be reported later.)

TABLE 5. *Effect of added propene (p_i); at* 325°.

T	p_0 (mm.)	p_i (mm.)	10^4k_1 (sec.$^{-1}$)	10^4k_1 (sec.$^{-1}$; calc.)	T	p_0 (mm.)	p_i (mm.)	10^4k_1 (sec.$^{-1}$)	10^4k_1 (sec.$^{-1}$; calc.)
322°	239	97	3·44	3·35	322°	215	190	3·14	3·35
323	231	144	3·62	3·55	324	295	291	3·51	3·80
324	216	146	3·54	3·80					

The results of the runs in the presence of added propene (pressure p_i) are shown in Table 5. There is a slight tendency for the rate to be less in the presence of added propene, but the experimental scatter precludes quantitative conclusions. It is obvious, however, that no

marked inhibition occurs and hence it may be concluded that the reaction is predominantly non-chain in character. This conclusion is borne out by the experiments in the presence of added *cyclo*hexene (see Table 6), the mean values of k in its absence and presence being $4{\cdot}05 \times 10^{-4}$ and $3{\cdot}75 \times 10^{-4}$ sec.$^{-1}$, respectively.

TABLE 6. *Effect of added* cyclo*hexene, at* 325°.

p_0 (mm.)	209	280	418	455	328	299	260	240	310
p_i (mm.)	0	0	0	0	110	120	130	140	200
10^4k_1 (sec.$^{-1}$)	3·97	4·10	4·16	3·97	3·73	3·80	3·67	3·75	3·82

DISCUSSION

The experimental results may be summarised as follows: (*a*) The pyrolysis of *sec.*-butyl bromide proceeds according to equation (4) in the temperature range 300—350°. (*b*) The reaction follows a first-order law, at least in the early stages where complications due to the reverse reaction may be neglected (for rate constants see above). (*c*) The first-order constants show no significant pressure variation over the range 25—350 mm. initial pressure. (*d*) The rate of reaction in the initial stages is unaffected by the addition of *cyclo*hexene or propene. (*e*) Increasing the inhibitor pressures cause the rate to depart from the first-order law at an earlier stage in the reaction.

The first-order rate law is consistent with a mechanism involving unimolecular elimination of hydrogen bromide, and with a chain mechanism involving bromine atoms, initiated by the breaking of the C–Br bond, but the latter is excluded by factor (*d*) above.

The effect (*e*), for *iso*propyl bromide, was attributed to the equilibrium $C_3H_7Br \rightleftharpoons C_3H_6 + HBr$. This phenomenon will in the present work be complicated by competition between the reactions, $C_4H_8 + HBr \rightleftharpoons C_4H_9Br$, and $C_3H_6 + HBr \rightleftharpoons C_3H_7Br$, or $C_6H_{10} + HBr \rightleftharpoons C_6H_{11}Br$. It is also found that the effect is not so marked as with *iso*propyl bromide.

The structure of the butene produced has not been studied. In the case of the chain mechanism, it appears likely that attack would be upon the secondary group, leading to but-2-ene. However, since little is as yet known about the effect of structure upon parameters of the Arrhenius equation for the unimolecular elimination, no definite conclusion can be drawn. It is perhaps suggestive that the activation energy is less than for *iso*propyl bromide, which may be due to energy differences between elimination involving hydrogen from secondary and primary groups.

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Studies in the Pyrolysis of Organic Bromides. Part V. The Pyrolysis of* cyclo*Hexyl Bromide.*†

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From 300° to 350°, in seasoned vessels, *cyclo*hexyl bromide decomposes homogeneously in the gaseous phase into *cyclo*hexene and hydrogen bromide according to a first-order law. Departures from this law after about 40% decomposition have been attributed to the incursion of the back-reaction. Rate constants for the initial stages of the reaction were fitted to the expression $k_1 = 3{\cdot}24 \times 10^{13} \exp(-46{,}100/RT)$ (sec.$^{-1}$). On the basis of this evidence and of the inability of *cyclo*hexene to inhibit the reaction, the mechanism is identified as unimolecular elimination of hydrogen bromide. No significant decrease in the rate constants with decreasing initial pressure was observed in the range 400—40 mm.

No previous studies have been made of the kinetics of pyrolysis of *cyclo*hexyl bromide in the gaseous phase. This compound was of interest to the present series of investigations as both the C–H and the C–Br bonds to be broken in the elimination of hydrogen bromide occur in secondary groups (cf. *sec.*-butyl bromide, Part IV *). It is also of interest to see the effect of the cyclic structure upon the rate. By analogy with the secondary bromides already studied, it might be expected that *cyclo*hexyl bromide would decompose cleanly into *cyclo*hexene and hydrogen bromide by a unimolecular reaction.

Experimental

*cyclo*Hexyl bromide (commercial) was freed from the alcohol by shaking with 60% aqueous hydrogen bromide, the excess of acid was then removed, and the sample dried and fractionated under a vacuum. It then had b. p. 72°/29 mm., n_D^{25} 1·4934 [cf. b. p. 71—72°/32 mm. (Beilstein's "Handbuch"), n_D^{25} 1·4935 (Heston, Hennelly, and Smythe, *J. Amer. Chem. Soc.*, 1950, **72**, 2071)].

A commercial sample of *cyclo*hexene was shaken with portions of aqueous ferrous sulphate to remove peroxides until no further change occurred. It was then washed with water, dried ($CaCl_2$), and fractionated at atmospheric pressure. It was stored in the dark over solid potassium hydroxide. It had b. p. 82·0°, n_D^{25} 1·4439 [cf. b. p. 82·3° (Pink and Ubbelohde, *Trans. Faraday Soc.*, 1948, **44**, 710), 83° (Timmermanns, "Physical Constants of Pure Organic Compounds," Elsevier, 1950), n_D^{25} 1·4437 (*op. cit.*)]. Analysis, by a method to be described later, showed it to be at least 99·2% pure.

Stoicheiometry of the Reaction.—Confirming the analogy with previous work on the alkyl bromides, it was verified that the products of pyrolysis were *cyclo*hexene and hydrogen bromide, and the reaction was conveniently measurable at 300° in a clean-walled reaction vessel. The ratio of final to initial pressure was always less than the value of 2 predicted from (1), owing to equilibrium between *cyclo*hexyl bromide and its decomposition products. The reaction appeared to be fairly clean, insofar as all the gases produced were condensed at liquid air temperatures. If the reaction is

$$C_6H_{11}Br \longrightarrow C_6H_{10} + HBr \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

then the amount of decomposition can be obtained from a knowledge of the initial pressure (p_0) and the pressure at time t (p_t)

$$\text{Decomposition (\%)} = 100\,(p_t - p_0)/p_0$$

This value can be compared with that obtained by direct titration of the hydrogen bromide produced.

The analytical procedure was varied slightly from that described in Part I (*J.*, 1955, 965). A known weight of *cyclo*hexyl bromide was introduced into the reaction vessel and after a given

* Part IV, preceding paper. † A preliminary report of the Arrhenius parameters for this reaction has already been given (*J. Chem. Phys.*, 1953, **21**, 178).

time the total pressure was noted and the products were condensed under a vacuum into a tube of *ca.* 200 c.c. capacity and sealed off. The tip of the tube was then broken under standard alkali and titrated as described previously. The results of such an investigation are shown in Fig. 1, in which the percentage decomposition found from an analysis for acid produced is plotted against that obtained from pressure measurements. The points all lie close to the line of unit slope, as would be expected from equation (1).

It was thought desirable to investigate the *cyclo*hexene–hydrogen bromide ratio, by analysis for both constituents in a single run. The *cyclo*hexene was estimated by bromine absorption, the most satisfactory results being obtained by the use of standard bromate–bromide. The procedure used was essentially that of Mulliken and Wakeman (*Ind. Eng. Chem., Anal.*, 1935, **7**, 59) who recorded that it tended to give low results. This observation was confirmed by Lucas and Pressman (*ibid.*, **1938**, **10**, 140), who developed a technique with added mercuric sulphate which, however, in the case of *cyclo*hexene, did not appear to improve the results. Typical

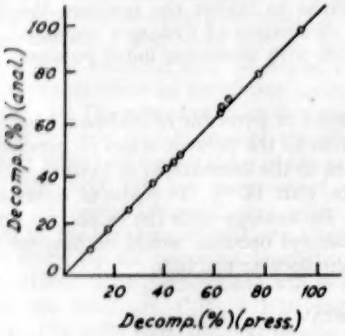


FIG. 1. *Percentage decomposition determined from pressure measurements and from a direct determination of the hydrogen bromide produced.*

results were: *cyclo*hexene taken 0·1042, 0·0845 g.; found 0·1033, 0·0839 g. For the analysis of *cyclo*hexene from the kinetic runs, the solution of the olefin in carbon tetrachloride was added to the bromate–bromide solution and the usual procedure followed. The results are shown in Table 1.

TABLE 1.

Temp.	295°	335°	327°	345°	323° *	355° *
Decomp. (%)	25·3	45·5	63·1	78·3	66·0	97·0, 98·0
C_6H_{10} : HBr	0·96	1·02	1·04	0·98	0·96	1·06, 0·98

* Sealed-tube technique.

The results presented in Fig. 1 and Table 1 give reasonable proof of the stoicheiometry represented by (1).

Independent evidence of the stability of *cyclo*hexene at the temperature used comes from the work of Küchler (*Nach. Akad. Wiss. Göttingen, Math.-phys. Kl.*, 1939, **1**, 231) who studied the decomposition and showed it to be

$$C_6H_{10} \longrightarrow C_4H_6 + C_2H_4.$$

This reaction is the reverse of a diene synthesis. The first-order rate constant was expressed as $k = 9{\cdot}0 \times 10^{12} \exp(-57{,}500/RT)$ (sec.$^{-1}$). At 350° this gives a half-life of 100 days. Rowley and Steiner (*Discuss. Faraday Soc.*, 1951, **10**, 198) suggest that the activation energy may even be as high as 64 kcal. So the secondary decomposition of *cyclo*hexene may be ignored in the present work.

RESULTS

The reaction was studied by measuring the rate of pressure increase as described in Part I (*loc. cit.*). It was found to follow a first-order law up to about 40% decomposition, the first-order constants being independent of initial pressure. As the reaction proceeded, the first-order constants fell, which can be ascribed to the reverse reaction, $C_6H_{10} + HBr \longrightarrow C_6H_{11}Br$. Preliminary runs in a clean-walled reaction vessel gave highly irreproducible results. In particular, traces of oxygen catalysed the reaction. On careful exclusion of oxygen, a gradual decrease in rate was observed. Thus in six runs at 304° the first-order constant dropped from $4{\cdot}3 \times 10^{-4}$ to $2{\cdot}2 \times 10^{-4}$ (sec.$^{-1}$). When the vessel was "seasoned" with the products of

pyrolysis of allyl bromide (Part II, *J.*, 1955, 973) the rate dropped to $1{\cdot}13 \times 10^{-4}$ sec.$^{-1}$, and the behaviour of *cyclo*hexyl bromide became reproducible.

To test the homogeneity of the reaction under these conditions, the surface : volume ratio was increased by a factor of about three, and no significant change in the rate was observed (see Table 2). Within the limits of experimental error the reaction is essentially homogeneous.

TABLE 2. *Effect of surface : volume ratio.*

Temp.	304°	309·5°	347·7°	349·4°
Surface : vol., 1·07 (cm.$^{-1}$) : 10^4k (sec.$^{-1}$)	1·17	1·62, 1·69	18·6	20·6
Surface : vol., 2·83 (cm.$^{-1}$) : 10^4k (sec.$^{-1}$)	1·10	1·76, 1·71	18·9	19·1

The lack of dependence of the first-order rate constants on initial pressure is illustrated for a series of runs at 327° in Table 3.

TABLE 3. *Effect of initial pressure, at* 327°.

p_0 (mm.)	435	362	333	275	247	245	203
10^4k_1 (sec.$^{-1}$)	5·04	5·34	4·90	4·65	4·73	5·26	4·93
p_0 (mm.)	195	165	134	80	75	64	40
10^4k_1 (sec.$^{-1}$)	4·81	5·44	5·42	5·50	4·60	5·38	5·60

The temperature dependence of the rate constant, determined from the means of a number of runs, is shown in Table 4. The variation of the rate constant with temperature was fitted to the Arrhenius equation $k_1 = 2{\cdot}4 \times 10^{13} \exp(-46{,}100/\boldsymbol{R}T)$ (sec.$^{-1}$), the results being shown graphically in Fig. 2.

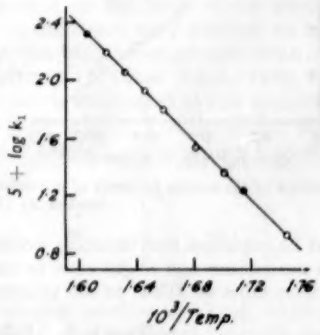


FIG. 2. *The Arrhenius plot. Black circles indicate runs in a packed vessel.*

In order to identify the mechanism, the decomposition was carried out in the presence of a number of added substances. *cyclo*Hexene should be a powerful inhibitor of chain reactions by virtue of the four C–H bonds adjacent to the double bond, the removal of any one of which would lead to a *cyclo*hexenyl radical. This should be comparable in stability to an allyl radical formed from propene and should readily remove bromine; so if bromine atom chains were present, inhibition should result. That no such inhibition results is shown in Table 5 (the

TABLE 4. *Temperature dependence.*

Temp.	350°	345°	340°	335°	330°	327°	322°	320°	315°	310°	300°
No. of runs ...	3 *	3	1	7	4	14	7	1	5	1 *	4
10^4k_1 (sec.$^{-1}$) ...	21·83	15·67	11·48	8·57	6·44	5·11	3·59	3·23	2·34	1·76	0·89

* In a packed vessel.

TABLE 5. *Effect of added* cyclo*hexene.*

Temp.	p_0 (mm.)	$p_{C_6H_{10}}$ (mm.)	10^4k_1 (sec.$^{-1}$) obs.	calc.	Temp.	p_0 (mm.)	$p_{C_6H_{10}}$ (mm.)	10^4k_1 (sec.$^{-1}$) obs.	calc.
313°	191	57	2·17	2·09	319·5°	230	264	3·30	3·22
316·8	175	52	2·84	2·72	324·5	217	139	4·33	4·47
316·8	228	145	2·42	2·72	326	192	123	4·68	4·92
317·2	201	129	2·57	2·76	326	217	251	4·92	4·92

calculated figures are obtained from the Arrhenius equation), and is definite evidence in view of the fact that P. J. Thomas (personal communication) has shown that *cyclo*hexene strongly

inhibits the pyrolysis of *n*-propyl bromide which has been shown (Part II, *loc. cit.*) to decompose according to a chain mechanism.

Since allyl bromide was used for producing seasoned walls, it was desirable to ascertain whether the addition of allyl bromide had an effect on the rate. At the temperature shown, allyl bromide decomposes with a half-life of about 150 min., whereas *cyclo*hexyl bromide has a

TABLE 6. *Rate constants in presence of allyl bromide* (15 mm.).

Temp.	330°	328°	328°	328°
p_0 (mm.)	220	308	245	325
10^4k_1 (sec.$^{-1}$) obs.	6·53	5·38	4·97	5·16
10^4k_1 (sec.$^{-1}$) calc.	6·57	5·72	5·72	5·72

half-life of about 20 min. The results are set out in Table 6 (calculated values from the Arrhenius plot). The course of the reaction was unchanged by the presence of allyl bromide and the first-order rate constants were essentially unaltered.

FIG. 3.

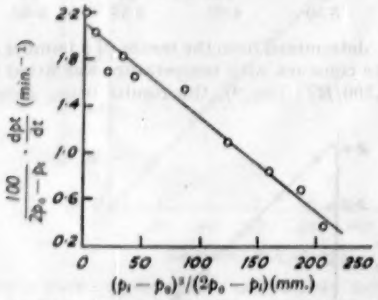
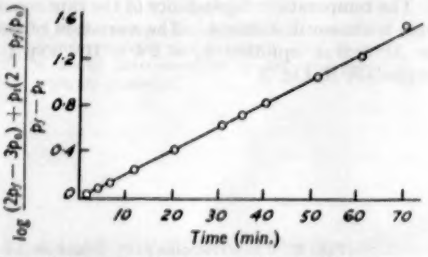


FIG. 4.



Interpretation of the results in terms of a combination of forward and reverse reactions: (FIG. 3, *method A*) (FIG. 4, *method B*).

It might be expected that bromine would accelerate a reaction proceeding by a bromine-atom chain mechanism and might even be capable of initiating such a route. For this reason some runs were done at 313·4° in the presence of varying pressures of bromine (see Table 7).

TABLE 7. *Effect of added bromine.*

p_0 (mm.)	163	251	140
p_{Br_2} (mm.)	6	13	30
10^4k_1 (sec.$^{-1}$)	2·1	1·89	2·59

The rate constant calculated from the Arrhenius plot for this temperature is $2{\cdot}14 \times 10^{-4}$ sec.$^{-1}$. Thus small pressures of bromine are without effect on the rate of decomposition of *cyclo*hexyl bromide. This result is paralleled by observations on *tert.*-butyl bromide (following paper).

During the work considerable qualitative evidence accumulated that the reaction did not go to completion. First, the values of p_f/p_0 were always less than the value 2 demanded by the reaction, $C_6H_{11}Br \longrightarrow C_6H_{10} + HBr$ (p_f = final pressure). Secondly, the logarithmic plots for the first-order rate constants deviated from a straight line to an extent dependent on pressure and temperature, the effect being more marked at high pressures and low temperatures. Thirdly, in the presence of added *cyclo*hexene, the deviations from linearity increased as the pressure of *cyclo*hexene increased. That the data are consistent with the scheme $C_6H_{11}Br \underset{k_2}{\overset{k_1}{\rightleftharpoons}} C_6H_{10} + HBr$ can be seen by applying the complete kinetic equation in either of two ways: in the differential form

$$(A) \qquad -\frac{1}{2p_0 - p_i} \cdot \frac{dp_i}{dt} = k_1 - k_2 \frac{(p_i - p_0)^2}{(2p_0 - p_i)}$$

or in the integrated form

$$(B) \qquad k_1 = \frac{p_f - p_0}{t(3p_0 - p_f)} \ln \frac{(2p_f - 3p_0) + p_i\,(2 - p_f/p_0)}{p_f - p_i}$$

p_0 is the initial pressure of *cyclo*hexyl bromide, p_t the total pressure at time t, and p_f the final pressure.

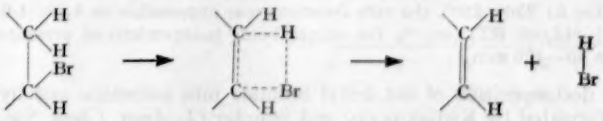
In method (*A*), $(2p_0 - p_t)^{-1}\mathrm{d}p_t/\mathrm{d}t$ was plotted against $(p_t - p_0)^2/(2p_0 - p_t)$, giving a straight line of slope k_2 and intercept k_1. This is shown in Fig. 3, the value of k_1 thus determined being $3{\cdot}5 \times 10^{-4}$ sec.$^{-1}$. k_1 is derived by method (*B*) from a plot of $\log\{[(2p_f - 3p_0) + p_t(2 - p_f/p_0)]/(p_f - p_t)\}$ against t, as shown in Fig. 4. The corresponding value of k_1 is $3{\cdot}78 \times 10^{-4}$ sec.$^{-1}$. These two values are to be compared with the value $3{\cdot}53 \times 10^{-4}$ sec.$^{-1}$ obtained from the initial slope of the conventional first-order plot. In both methods (*A*) and (*B*) the straight lines are reasonably good. Because of dead-space errors, it is not considered that reliable values of K_p could be derived from experiments in the present apparatus. It can, however, be concluded that the experimental results are in accord with an equilibrium between *cyclo*hexyl bromide and its decomposition products, lying well towards dissociation in the temperature range 300—350°.

Discussion

It has been established that the decomposition of *cyclo*hexyl bromide in the temperature range 300—350° proceeds homogeneously according to the scheme

$$C_6H_{11}Br \longrightarrow C_6H_{10} + Br$$

The reaction is of the first order and no pressure dependence of the constants has been observed in the pressure range 40—400 mm. *cyclo*Hexene has no effect on the rate; bromine very little. These facts can be interpreted on the basis of the mechanism *not* involving bromine atom chains; further such chains seem very difficult to induce. In view of the magnitude of the activation energy, the bromine-atom non-chain mechanism suggested for ethyl bromide by Daniels and Veltman (*J. Chem. Phys.*, **1939**, **7**, 756) and found by one of us for allyl bromide (Part I, *loc. cit.*) is eliminated as this leads to an activation energy equal to the C–Br bond strength (~60 kcal.). The remaining possibility is the unimolecular elimination of hydrogen bromide through a four-centre transition state:



The value of the activation energy found in the present work is 46·1 kcal., to be compared with the values 47·8 and 43·8 kcal. for *sec.*-propyl and *sec.*-butyl bromide respectively (Parts III and IV, *J.*, **1955**, 979, 2445). In all these cases the elimination proceeds by the breaking of C–H and C–Br bonds in secondary groups.

The observed value of the frequency factor ($2{\cdot}4 \times 10^{13}$ sec.$^{-1}$) is close to that found for a large number of unimolecular reactions (~10^{13}). Although a number of workers (for references see Slater, *Proc. Roy. Soc.*, **1948**, *A*, **194**, 112) have shown that the frequency

Table 8.

Halide	log *A*	*E* (kcal.)	Ref.
Elimination of hydrogen bromide.			
sec.-Propyl	13·62	47·8	Part III
sec.-Butyl	12·63	43·8	„ IV
tert.-Butyl	13·3	40·5	K. & S.*
„	14·00	42·2	Part VI
*cyclo*Hexyl	13·38	46·1	This work
Elimination of hydrogen chloride.			
Ethyl	14·6	60·8	1
n-Propyl	13·5	55·0	2
sec.-Propyl	13·4	50·5	3
n-Butyl	14·0	57·0	2
tert.-Butyl	13·9, 12·4	45·0, 41·4	4, 5

* Kistiakowsky and Stauffer, *J. Amer. Chem. Soc.*, 1937, **59**, 165.
[1] Barton and Howlett, *J.*, 1949, 155. [2] Barton, Head, and Williams, *J.*, 1951, 2039. [3] Barton and Head, *Trans. Faraday Soc.*, 1950, **46**, 114. [4] Brearly, Kistiakowsky, and Stauffer, *J. Amer. Chem. Soc.*, 1936, **58**, 44. [5] Barton and Onyon, *Trans. Faraday Soc.*, 1949, **45**, 725.

factor should be of the order of 10^{13} when a single bond breaks, the extension of the argument to the four-centre case is not immediately obvious. In fact Glasstone, Laidler, and Eyring ("Theory of Rate Processes," McGraw-Hill, New York, 1941) have suggested that in this type of reaction the frequency factor should be low, corresponding to a higher degree of organisation in the transition state. This view is certainly not borne out in elimination reactions involving the formation of a double bond, as Table 8 shows. It may be that, because of restricted rotation in the initial state, the change in the degree of organisation on going to the transition state is slight.

The authors acknowledge their indebtedness to Professor C. K. Ingold, F.R.S., for his interest, and to Dr. P. J. Thomas for many discussions. One of them (J. H. S. G.) acknowledges the award of a D.S.I.R. Maintenance Grant.

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Studies in the Pyrolysis of Organic Bromides. Part VI. The Pyrolysis of* tert.*-Butyl Bromide.†*

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[Reprint Order No. 5997.]

The present investigation confirms Kistiakowsky and Stauffer's observation that *tert.*-butyl bromide decomposes by a unimolecular mechanism in seasoned reaction vessels. This was achieved by observing the lack of inhibition of the decomposition in the presence of *cyclo*hexene and *cyclo*pentadiene. Further, allyl bromide and bromine were ineffective in stimulating a chain decomposition. Oxygen had a powerful accelerating effect. At 230—280°, the rate constant was expressible as $k_1 = 1{\cdot}0 \times 10^{14} \exp(-42{,}000/\boldsymbol{R}T)$ (sec.$^{-1}$), the values being independent of pressure in the range 40—400 mm.

THE thermal decomposition of *tert.*-butyl bromide into *iso*butene and hydrobromic acid has been investigated by Kistiakowsky and Stauffer (*J. Amer. Chem. Soc.*, 1937, **59**, 165) in the temperature range 235·7—291·6°. They concluded that the reaction was homogeneous and of the first order, with a velocity constant $k_1 = 10^{13\cdot3} \exp(-40{,}500/\boldsymbol{R}T)$ (sec.$^{-1}$), and that the mechanism involved was a unimolecular loss of hydrogen bromide. It seemed desirable, in connection with the present investigations, first, to study the reaction under conditions similar to those obtaining for the other bromides and, secondly, to ascertain whether the reaction could be inhibited.

EXPERIMENTAL

tert.-Butyl bromide was prepared by the hydrogen bromide–sulphuric acid method suggested by Bryce-Smith and Howlett (*J.*, 1951, 1141). Its b. p. was 73·1°/767 mm. (Timmermans, "Physical Constants of Pure Organic Compounds," Elsevier, 1950, gives b. p. 73·25°/760 mm.), and n_D^{25} was 1·4250 (Bryce-Smith and Howlett, *loc. cit.*, give n_D^{25} 1·4249). The pure bromide was stored over silver wire in the dark.

The experimental technique was essentially as described in Part I (*loc. cit.*). The bromide was admitted to the reaction vessel from a vapour reservoir. No direct investigation of the stoicheiometry of the reaction was possible, since the products recombined during the condensation. By analogy with the other bromides studied, the reaction is almost certainly:

$$C_4H_9Br \longrightarrow C_4H_8 + HBr$$

the olefin being *iso*butene. This overall reaction received confirmation from three sources. First, the final pressure (p_f) approached a value of twice the initial (p_0) (see Table 1): it is

* Parts I—III: *J.*, 1955, 965, 973, 979. Parts IV and V, preceding papers.

† The Arrhenius parameters reported in this paper have previously been referred to (*J. Chem. Phys.*, 1953, **21**, 178).

TABLE 1. *Stoicheiometry.*

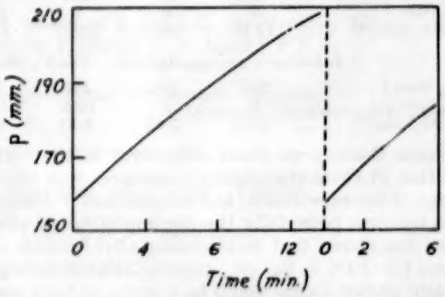
Temp.	p_0 (mm.)	p_f (mm.)	p_f/p_0	Temp.	p_0 (mm.)	p_f (mm.)	p_f/p_0	Temp.	p_0 (mm.)	p_f (mm.)	p_f/p_0
277·9°	144	268	1·86	276·6°	218	403	1·85	268·6°	149	284	1·91
277·5	236	431	1·83	268·8	220	400	1·82	252·7	200	366	1·83
277·5	218	406	1·86	268·8	213	391	1·84	238·6	268	492	1·84
277·5	224	418	1·87								

somewhat less than two because (*a*), as shown by Kistiakowsky and Stauffer (*loc. cit.*), an equilibrium was set up between *tert.*-butyl bromide, *iso*butene, and hydrogen bromide, and (*b*), by virtue of the dead space inherent in the vessel used, the final pressure is not expected to reach the value $2p_0$ (Allen, *J. Amer. Chem. Soc.*, 1934, **56**, 2053). Secondly, no non-condensable

TABLE 2.

Temp.	p_0 (mm.)	10^4k_1 (sec.$^{-1}$)	p_f (mm.)	p_0' (mm.)	$10^4k_1'$ (sec.$^{-1}$)
276·0°	114	13·9	167·5	118	13·7
259·4	158	4·78	208	158	4·99

gases were produced. Thirdly, when the products were condensed out and then readmitted to the reaction vessel, not only were the original initial pressures reproduced, but also the rate of decomposition : this behaviour is illustrated in Table 2, where p_0 and k_1 refer to the initial runs and p_0' and k_1' to the runs after condensation (at p_f) and readmission. The behaviour is so



Pressure–time curve, showing the essential reversibility of the reaction. The reaction was stopped and then restarted, at the broken line.

striking that a pressure–time curve is reproduced in the Figure. Of the three butenes that could be produced, only *iso*butene would give *tert.*-butyl bromide on recombination. As the kinetic studies show that *tert.*-butyl bromide is in fact produced, it follows that the olefin formed must have been *iso*butene.

Some preliminary runs were carried out in a clean-walled Pyrex vessel at 258·5° and 272·9°. In no case was a change of pressure with time observed. A weighed sample of *tert.*-butyl bromide was then admitted to the system, and, after 90 sec. the pressure was 440 mm., whereas the calculated initial pressure was about 180 mm. This shows that the reaction is very fast in clean Pyrex vessels. The remainder of the runs were done in a Pyrex reaction vessel which had been seasoned by the pyrolysis products of allyl bromide.

In order to check the first-order character of the decomposition, a series of runs were done at 276·6°, with initial pressures varying from 48 to 446 mm. The rate constants derived are shown in Table 3. The first-order rate constants varied by a maximum of ±6% from the mean value,

TABLE 3.

p_0 (mm.)	$10^3k_{0\cdot5}$ (mm.$^{\frac{1}{2}}$ sec.$^{-1}$)	10^4k_1 (sec.$^{-1}$)	$10^3k_{1\cdot5}$ (mm.$^{-\frac{1}{2}}$ sec.$^{-1}$)	p_0 (mm.)	$10^3k_{0\cdot5}$ (mm.$^{\frac{1}{2}}$ sec.$^{-1}$)	10^4k_1 (sec.$^{-1}$)	$10^3k_{1\cdot5}$ (mm.$^{-\frac{1}{2}}$ sec.$^{-1}$)
446	32·00	15·91	7·03	217·5	22·00	16·63	10·20
379	33·33	16·67	8·93	150·5	21·33	17·62	14·47
294·5	28·67	16·85	9·93	123·6	17·33	16·89	14·50
247	26·67	16·97	11·20	91·0	14·13	17·06	16·00
218	22·67	15·78	10·73	48·3	11·20	17·62	23·33

but no systematic trend was observable. In view of the fact that Kistiakowsky and Stauffer (*loc. cit.*) had reported the homogeneous nature of the decomposition, it was not thought necessary to measure the rates in packed vessels.

The variation of the rate constants with temperature was determined in the range 231—284°: see Table 4. From the plot of log k against the reciprocal of the absolute temperature, the rate was found to be expressible as $k = 10^{14\cdot9} \exp(-42{,}000/RT)$ (sec.$^{-1}$).

TABLE 4.

No. of runs	Temp.	10^4k_1 (sec.$^{-1}$)	No. of runs	Temp.	10^4k_1 (sec.$^{-1}$)	No. of runs	Temp.	10^4k_1 (sec.$^{-1}$)
5	282·4°	24·25	3	266·1°	7·68	3	243·3°	1·31
6	280·7	21·31	10	261·5	5·51	4	240·0	1·09
10	276·6	16·80	6	255·6	3·41	3	235·5	0·709
7	272·9	12·41	4	255·1	3·33	4	231·2	0·467
5	272·2	12·27	3	247·9	1·94			

The main purpose of the work described here was to examine the reaction in the presence of inhibitors, to verify whether or not the reaction proceeds by a unimolecular elimination. Two inhibitors were used, *cyclo*hexene and *cyclo*pentadiene, both having been found by P. J. Thomas (personal communication) to be highly efficient in inhibiting the chain mechanism in the decomposition of *n*-propyl bromide (cf. Part II). Only a single temperature was used in each case. The results, shown in Table 5, p_i representing the pressure of inhibitor, give no evidence of inhibition, within the limits of experimental error.

TABLE 5.

	Inhibitor: cyclo*hexene*. *Temp.*, 273·2. $k_{calc.} = 12{\cdot}47 \times 10^{-4}$ (sec.$^{-1}$).							
p_0 (mm.)	302	259	288	305	249	311	303	316
p_i (mm.)	0	0	7	19·5	32	34	40·5	41·5
10^4k_1 (sec.$^{-1}$)	12·48	12·67	12·57	12·33	12·95	12·44	11·72	12·79

	Inhibitor: cyclo*pentadiene*. *Temp.*, 265·7°. $k_{calc.} = 7{\cdot}28 \times 10^{-4}$ (sec.$^{-1}$).						
p_0 (mm.)	257	207	140	218	222	221	246
p_i (mm.)	0	0	10·5	54·5	87·5	98	121
10^4k_1 (sec.$^{-1}$)	6·99	7·49	6·91	6·72	6·97	7·22	6·95

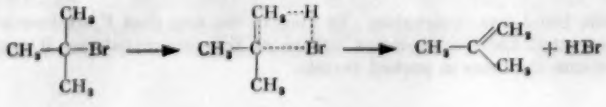
Since there is no chain component in the normal decomposition in seasoned vessels, the addition of chain-stimulating substances was tried. Molecular bromine provides an obvious source of bromine atoms, and Daniels and Veltman (*J. Chem. Phys.*, 1939, **7**, 756) have shown it to catalyse powerfully the decomposition of ethyl bromide. Thomas (personal communication) has shown that decomposing allyl bromide will also provide a concentration of bromine atoms (cf. Part I, *loc. cit.*) capable of stimulating a chain mechanism in bromide pyrolyses. Finally methyl iodide would be a source of both methyl radicals and iodine atoms, which might conceivably initiate reaction chains. The results of pyrolysis carried out in the presence of these substances, shown in Table 6 (the pressure of added stimulant is represented by p_s), provide no evidence of *tert.*-butyl bromide's supporting a radical-chain mechanism.

TABLE 6.

Stimulant: *molecular bromine*. *Temp.*, 264·4°. $k_{calc.} = 6{\cdot}70 \times 10^{-4}$ (sec.$^{-1}$).			*Stimulant*: *allyl bromide*. *Temp.*, 265·3°. $k_{calc.} = 7{\cdot}13 \times 10^{-4}$ (sec.$^{-1}$).			*Stimulant*: *methyl iodide*. *Temp.*, 266·5°. $k_{calc.} = 7{\cdot}76 \times 10^{-4}$ (sec.$^{-1}$).		
p_0 (mm.)	p_s (mm.)	10^4k_1 (sec.$^{-1}$)	p_0 (mm.)	p_s (mm.)	10^4k_1 (sec.$^{-1}$)	p_0 (mm.)	p_s (mm.)	10^4k_1 (sec.$^{-1}$)
304	0	6·83	352	0	6·82	281	0	7·25
206	0	6·81	306	52	6·77	227	0	7·87
252	19	6·93	276	53	6·80	243	36	7·81
220	44	6·49	167	68	6·55	275	45·5	7·79
367	46·5	6·72				147	56	7·60
						258	92·5	7·10

DISCUSSION

Pyrolysis of *tert.*-butyl bromide in the gaseous phase in seasoned reaction vessels has been shown to be a first-order, homogeneous reaction, as concluded by Kistiakowsky and Stauffer (*loc. cit.*). Further, the inability of established olefinic inhibitors to alter the rate may be taken as proof of the unimolecular nature of the reaction. There is little doubt that the reaction investigated takes place by the four-centre transition-state mechanism:



This type of mechanism has also been reported (Parts III—V) to occur with those compounds studied containing C–Br links in secondary groups, namely, *sec.*-propyl, *sec.*-butyl, and *cyclo*hexyl bromide. This sharply distinguishes the secondary and the tertiary from the primary compounds. It seems highly probable that ethyl bromide decomposes at least partially by a chain mechanism (Daniels and Veltman, *J. Chem. Phys.*, 1939, **7**, 756). Again it was shown in Part II that *n*-propyl bromide decomposes by a chain process. It is of interest that the relative rates of pyrolysis of *sec.*-propyl and *tert.*-butyl bromide at 360° are approximately 1 : 170, an extrapolated value being used for *tert.*-butyl bromide.

It should be noted that in the temperature range investigated, all the rates reported here are somewhat lower than those reported by Kistiakowsky and Stauffer. It is difficult to see any mechanism for retarding a strictly unimolecular decomposition, and so it is believed that the present parameters are the more reliable.

The other factor that emerges from this work is the inability to induce chains, even in the presence of a relatively high pressure of bromine, although all radicals produced by bromine atom attack are P-radicals in the nomenclature of Part III. This observation bears out the view put forward there that the production of chains depends at least in part upon ease of bromine atom attack on a C–H bond in a secondary group. Thus in *n*-propyl bromide, P-radicals are produced by an attack on a methylene group,* while in *sec.*-propyl bromide and *tert.*-butyl bromide they are only produced by an attack on a methyl group.

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The Thermal Decomposition of Silver Nitrite.

By T. M. Oza, V. T. Oza, and R. H. Thaker.

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Examination of the results of decomposition of silver nitrite alone, under different conditions, and with the addition of silver oxide has shown that the reaction $AgNO_2 = Ag + NO_2$ proceeds through the intermediate fast reaction $2AgNO_2 \rightleftharpoons Ag_2O + N_2O_3 (= NO + NO_2)$. Silver oxide has been isolated by carrying out the decomposition in oxygen. Experiments were also carried out on the mutual effect of the substances present (or formed) in the system; *e.g.*, the effect of (*a*) nitric oxide and (*b*) nitrogen dioxide on (i) silver oxide and (ii) silver nitrite and of nitric oxide on silver nitrate. The equilibrium $AgNO_2 + NO \rightleftharpoons AgNO_3 + NO_2$ was isolated; this reaction replenishes the nitrite and is fairly rapid under the experimental conditions so that it arrests the formation of nitrogen as $AgNO_2 + NO = AgNO_3 + \frac{1}{2}N_2$ by preventing the access of nitric oxide to nitrite. Formation of silver nitrate seems to occur by $AgNO_2 + O = AgNO_3$ though some of it is formed also by $Ag_2O + NO_2 = AgNO_3 + Ag$; the oxygen comes, at 130°, when the dissociation of nitrogen dioxide is absent, from silver oxide. No evidence is found for the reaction $Ag_2O + 2NO_2 = AgNO_3 + AgNO_2$ which is characteristic of wet systems.

Divers (*J.*, 1871, **24**, 85) found that silver nitrite fused at 134° in air and evolved a reddish gas at 150°. He thought the reaction (1) $3AgNO_2 = 2Ag + AgNO_3 + N_2O_3$ occurred below 134° and represented the ultimate changes as (2) $2AgNO_2 = Ag + AgNO_3 + NO$, as he found neither silver oxide nor nitrogen in the decomposition products. Divers and Schimidzu (*J.*, 1885, **47**, 630) found that silver nitrate, unmixed with nitrite, was formed by the action of nitrogen dioxide on reduced spongy silver. They also heated silver

* Unpublished work on *iso*butyl bromide in which P-radicals are produced by attack on a tertiary group suggests that such an attack is still readier, leading apparently to very long chains.

nitrite with nitrogen dioxide at 125° for 15 hr. and found that half the nitrite was oxidized to nitrate; however, they believed that silver nitrate was formed by the action of nitrogen dioxide on silver (5, below) and not on silver nitrite. Oswald, on the other hand (*Compt. rend.*, 1911, **152**, 381), supposed that nitrate was formed as (3) $AgNO_2 + NO_2 = AgNO_3 + NO$. Ray and Ganguli (*Proc.*, 1905, **21**, 279) found their two varieties of silver nitrite to decompose differently according to (4) α-$AgNO_2 = Ag + NO_2$ with a side reaction (5) $Ag + N_2O_4 = AgNO_3 + NO$, and (6) β-$AgNO_2 = Ag + O + NO$. Tzentnershver and Checinski (*Bull. Intern. Acad. Polonaise, Classe Sci. math. nat.*, 1935, *A*, **156**) studied the thermal dissociation of silver nitrite, and Blumenthal and Checinski (*ibid.*, p. 165) studied the kinetics of the dissociation. The former found that the dissociation occurred as (7) $AgNO_2 = Ag + NO_2 - 18{,}900$ cal. and (8) $2AgNO_2 = Ag + AgNO_3 + NO - 15{,}500$ cal., and regarded formation of nitrate as the primary change; the latter found that (7) was complete at 195°/2 mm. but (8) was incomplete at 195°/753 mm.; further that (7) was reversible at room temperature and that (8) went almost to completion. Checinski and his co-workers thought that the reactions in the decomposition occurred as in (4) and (5) and that they were of first order at low pressures and of second order under atmospheric pressure. Randall, Manov, and Brown (*J. Amer. Chem. Soc.*, 1938, **60**, 694) used the equation $2AgNO_2(s) = Ag(s) + AgNO_3(s) + NO(g)$ to compute the heat capacities of the substances concerned: their silver nitrite decomposed at 101·6°.

We now describe experiments on the decomposition of pure silver nitrite, *in vacuo*, under different conditions, alone and with the addition of silver oxide. The products of the reaction were quantitatively examined at various stages with a view to collect evidence for the transitory formation of silver oxide. Experiments were then done to examine the mutual effect of the substances present (or formed) in the system: *e.g.*, the action of (*a*) nitric oxide and (*b*) nitrogen dioxide on silver oxide and on silver nitrite; and of nitric oxide on silver nitrate. Finally silver oxide was isolated by conducting the decomposition at 130° in an atmosphere of oxygen (11 cm. pressure).

Experimental

Materials.—Silver nitrite was prepared from pure sodium nitrite and silver nitrate, recrystallized, dried in a desiccator (H_2SO_4), pulverized, and kept in a desiccator in the dark (Found: Ag, 70·1; NO_2', 29·9. Calc. for $AgNO_2$: Ag, 70·1; NO_2', 29·9%). Silver oxide was prepared from very dilute solutions of the nitrate and potassium hydroxide, and the dark grey precipitate washed freely with water, and dried in vacuum desiccator (H_2SO_4) (Found: Ag, 93·2. Calc. for Ag_2O: Ag, 93·1%). Nitric oxide was obtained by heating pure silver nitrite and absorbing the gases in alkali: it was all absorbed in alkaline sulphite. Pure dinitrogen tetroxide was prepared according to Addison, Gamlen, and Thompson (*J.*, 1953, 338); after fractionation it was collected in tubes of 4—6 mm. diameter, drawn out to a capillary at one end, and sealed: it was completely absorbed in concentrated potassium hydroxide solution producing equivalent amounts of nitrite and nitrate. Silver metal was obtained from silver nitrate solution by displacement with pure copper, washed, pulverized, analysed (found pure), and stored. Oxygen was prepared from potassium chlorate in a T system closed by a tap.

The apparatus used for studying decomposition was as described by Oza and Oza (*J.*, 1953, 908), a T-piece carrying the tube containing potassium chlorate plugged by glass wool and provided with a tap being attached in experiments in oxygen (Table 8). The experiments with dinitrogen tetroxide were done in the apparatus shown in Fig. 1: *d* is the tetroxide tube, previously weighed, and inserted with its capillary elongation inside the bore of key of the stopcock, *A*. The substance (oxide or nitrite) was weighed and placed in *T*, and *B* was heated in a bath for ½ hr. at the temperature of the experiment before the tetroxide tube was broken. *P* (or *Q*) was cooled in an ice-bath, and nitrogen dioxide was passed over the substance in *T* by alternately cooling and warming *P* and *Q*. Phosphoric acid was placed in *C* before the start of each experiment and the apparatus evacuated and allowed to stand for 1 hr.; *b'* was then turned off, phosphoric oxide removed, and potassium hydroxide solution placed in *C*, *D*, and *E*. By turning *A*, the capillary of tetroxide tube *d* was broken, and gas released: the glass was collected at the end of the experiment and weighed to get the weight of tetroxide taken at the start. The apparatus used for studying the effect of nitric oxide is shown in Fig. 2; *B* is a bulb

(100 c.c.) to contain (weighed) silver oxide, nitrite, or nitrate between taps T_1 and T_2. The pressure of the pure nitric oxide, produced on the left of T_1, is noted on the Sprengel pump through the upper branch of T_2; T_1 and T_2 are closed, gas to the right of T_2 pumped out, and heating of B started. At the end, the gas is collected in aqueous potassium hydroxide (lower branch of T_2), and nitrogen dioxide determined by analysing the alkali for nitrite.

Analyses.—The residue, examined for nitrite, nitrate, silver, and silver oxide, showed the absence of the last in all experiments except those of Table 8: it was extracted with hot water till no silver ions passed into solution and made up to a known volume (A): the solution was alkaline in those experiments of Table 8 which show the presence of silver oxide. The insoluble portion (Ag) was dissolved in hot dilute (1 : 1) nitric acid, boiled till no nitrous fumes were evolved, and diluted to a known volume (B). A and B were analysed for silver by Volhard's method, and A also for nitrite and nitrate (Oza and Oza, *loc. cit.*); the silver in A less that equivalent to nitrite and nitrate found gave that equivalent to Ag_2O. The gas pumped off was analysed for nitric oxide and nitrogen, nitrogen dioxide being absorbed with its equivalent

FIG. 1.

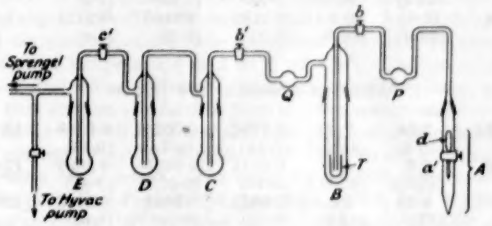
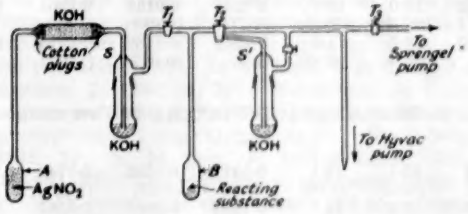


FIG. 2.



nitric oxide in alkali (in the apparatus) and determined as nitrite ($2KOH + N_2O_3 = 2KNO_2 + H_2O$). When nitric oxide was absent, the gas was tested for oxygen and, if this was present, absorbed in alkaline pyrogallol. Nitric oxide was absorbed in alkaline sulphite. All recorded volumes are at N.T.P.

Results.—To find the initial temperature of decomposition of silver nitrite 0·35 g. of it was kept *in vacuo* surrounded by an oil-bath and heated for ½ hr. at 50°; the temperature was then raised by 10°/10 min. to 100°; it was kept at 102—103° for 1 hr. (Randall, Manov, and Brown, *loc. cit.*) and then raised by 5°/10 min. Decomposition occurred at 128°.

For experiments at 480° heating was done electrically and the temperature was constant to within ±5°; for others, in an oil-bath, the temperature was controlled mechanically to within ±1°.

Table 1 contains results of experiments on the effect of time, mass, and temperature on the decomposition. They show the presence of nitric oxide and nitrogen dioxide in the gaseous and of silver and silver nitrate in the solid products; no nitrogen or oxide was present in any case. Expts. 1—8 were done with 0·35 g. of nitrite, at 130°, for varying times and show a greater rate of decomposition during the first 2 hr. in which the proportion of nitrogen dioxide increases and that of nitric oxide diminishes slowly; after 2 hr. the proportions are reversed. The ratio $Ag : AgNO_2$(consumed) is fairly constant, while the trends of the ratios $Ag : AgNO_3$ and $AgNO_3$(consumed) : $AgNO_3$, which are similar (low at first, sudden increase to maximum at 2 hr., steady fall), are dissimilar to those of $Ag : AgNO_2$(consumed). This shows that per unit of silver nitrite decomposed, formation of silver is steady but that of silver nitrate is not, *i.e.*,

TABLE 1. *Effect of time, mass, and temperature upon the decomposition of silver nitrite.*

(a) Effect of time at 130° on 0·35 g. of silver nitrite.

Expt. No.	Duration (hr.)	Gas evolved (c.c. at N.T.P.) * Total	NO	NO_2	Solid products: Ag †	$AgNO_2$ †	$AgNO_2$ used †	Ag / $AgNO_2$	Ag / $AgNO_2$	$AgNO_2$ / $AgNO_2$
1	½	2·83	1·66	1·15	0·0094	0·00307	0·0151	4·81	0·887	5·43
			(59·3)	(40·6)	(0·087)	(0·018)	(0·098)			
2	1	6·90	4·03	2·87	0·0267	0·0041	0·0457	10·25	0·832	12·32
			(58·4)	(41·6)	(0·247)	(0·024)	(0·297)			
3	2	14·02	8·12	5·9	0·0632	0·0081	0·0973	12·29	0·926	13·26
			(57·9)	(42·1)	(0·58)	(0·048)	(0·63)			
4	4	17·28	10·58	6·7	0·0788	0·0142	0·1256	8·76	0·895	9·76
			(61·2)	(38·8)	(0·73)	(0·083)	(0·82)			
5	6	18·98	11·57	7·4	0·0858	0·0210	0·1414	6·4	0·865	7·4
			(60·9)	(39·1)	(0·79)	(0·124)	(0·92)			
6	8	20·5	12·5	8·00	0·0945	0·0260	0·1572	5·72	0·858	6·67
			(61·0)	(39·0)	(0·87)	(0·15)	(1·0)			
7	10	23·00	14·1	8·9	0·1067	0·0315	0·1808	5·34	0·837	6·38
			(61·3)	(38·7)	(0·9)	(0·18)	(1·2)			
8	12	25·8	16·5	9·3	0·1183	0·0486	0·2125	3·86	0·797	4·83
			(64·0)	(36·0)	(1·1)	(0·29)	(1·4)			

(b) Effect of mass at 130° in 2 hr.

	Mass (g.)									
9	0·1098	4·03	2·04	1·99	0·0192	0·00242	0·0296	12·4	0·927	13·4
			(50·6)	(49·4)	(0·18)	(0·014)	(0·19)			
10	0·2405	9·9	5·6	4·3	0·0451	0·0055	0·0693	12·9	0·929	13·9
			(56·2)	(43·8)	(0·42)	(0·032)	(0·45)			
11	0·3526	14·02	8·12	5·9	0·0632	0·0081	0·0973	12·3	0·926	13·3
			(57·9)	(42·1)	(0·58)	(0·048)	(0·63)			
12	0·4814	22·22	13·1	9·1	0·1075	0·0110	0·1639	15·35	0·930	16·5
			(58·8)	(41·2)	(0·99)	(0·065)	(1·1)			
13	0·6006	26·12	16·0	10·1	0·1247	0·0138	0·1901	14·2	0·927	15·3
			(61·3)	(38·7)	(1·1)	(0·081)	(1·2)			
14	0·7210	30·03	18·1	11·9	0·1349	0·0166	0·2073	12·8	0·926	14·0
			(60·4)	(40·6)	(1·2)	(0·097)	(1·3)			

(c) Effect of time at 230° on 0·26 g. of silver nitrite.

	Duration (min.)									
15	8	20·3	10·1	10·1	0·0972	0·0393	0·1742	3·88	0·796	4·87
			(50·0)	(50·0)	(0·90)	(0·23)	(1·1)			
16	15	27·5	12·8	14·7	0·1293	0·0501	0·2362	4·1	0·779	5·2
			(46·5)	(53·4)	(1·2)	(0·29)	(1·5)			
17	45	30·9	14·1	16·8	0·1477	0·0516	0·2574	4·5	0·820	5·5
			(45·4)	(54·6)	(1·4)	(0·30)	(1·7)			
18	165	30·8	14·0	16·8	0·1474	0·0510	0·2570	4·5	0·814	5·6
			(45·4)	(54·6)	(1·4)	(0·30)	(1·7)			
19	285	,,	,,	,,	,,	,,	,,	,,	,,	,,
20	405	,,	,,	,,	,,	,,	,,	,,	,,	,,

(d) Effect of temperature on 0·35 g. of silver nitrite in 2 hr.

	Temp.									
21	130°	14·02	8·1	5·9	0·0632	0·0081	0·0973	12·3	0·926	13·3
			(57·9)	(42·1)	(0·58)	(0·048)	(0·63)			
22	170	26·7	17·3	9·4	0·1012	0·0337	0·1746	4·7	0·822	5·8
			(64·7)	(35·3)	(0·94)	(0·20)	(1·1)			
23	200	35·2	17·9	17·3	0·1628	0·0430	0·2723	6·0	0·853	7·00
			(50·9)	(49)	(1·5)	(0·25)	(1·8)			
24	220	39·1	19·6	19·5	0·1778	0·0527	0·3011	5·3	0·842	6·3
			(50·2)	(49·8)	(1·6)	(0·31)	(2·0)			
25	240	42·5	19·5	23·0	0·2052	0·0603	0·3471	5·4	0·841	6·4
			(45·9)	(54·1)	(1·9)	(0·35)	(2·3)			
26	480	52·7	21·6	28·1	0·2416	0·0085	0·3516	4·5	0·978	45·8
					(2·2)	(0·050)	(2·3)			

Plus O_2 = 3·0 c.c.

* Composition (%) is given in parentheses.
† Parentheses contain m moles or mg.-atoms.

silver nitrate is not a product of primary change as required by eqns. (1), (2), and (5). Expts. 9—15 show the effect of mass on the formation of the products: increase of mass diminishes the proportion of nitrogen dioxide but increases that of nitric oxide as when the latter is produced from the former. The ratio Ag : $AgNO_3$(consumed) is again constant, the value being comparable with that in expts. 1—8; the other two ratios, which amongst themselves show similar trends, have values similar to the value in the 2-hr. expt. (No. 3) when the mass is less than 0·35 g., but with a larger mass the value increases; it seems that the net silver nitrate production is greater in expts. 9—11 than in 12—14, and since in the latter expts. the amounts of nitric oxide and nitrogen dioxide are higher, it appears that silver nitrate is effectively reduced by nitric oxide: $AgNO_3 + NO = AgNO_2 + NO_2$ (Oza and Oza, *loc. cit.*). Expts. 15—20 show the effect of time at a higher temperature (230°) on a constant mass (cf. expts. 1—8): at 130° the decomposition was incomplete in 12 hr., but at 230° it is complete in 15 min. Expts. 17—20 show static conditions in the system although some nitrite is present even after 6¾ hr.; the rate of formation of nitrate is higher, as before, at first. At 480° (expt. 26) no nitrite is left. This shows that at 500—550°, the temperature used by Mehta (*Brit. Abs.*, 1942, I, 245), the rate of decomposition must be very great and the silver oxide, found by him, may have been formed by the interaction of silver in the system with atmospheric oxygen. The higher proportions of nitrogen dioxide in expts. 15—20 and smaller values of Ag : $AgNO_3$ and $AgNO_2$: $AgNO_3$, indicating enhanced nitrate formation, show formation of nitrate by nitrogen dioxide. Expts. 21—26 show the effect of temperature in 2 hr.: at 480°, when no nitrite is left, the system contains free oxygen and silver nitrate (which was steadily increasing in expts. 21—25) diminishes, showing that oxygen was formed from it: the system was exposed to alkali throughout, so that nitrous fumes were all absorbed and only surplus nitric oxide left. At 130° and 170° nitric oxide exceeds nitrogen dioxide; at 200—220°, the two are identical and at 240° and 480° nitrogen dioxide exceeds nitric oxide. The ratio Ag : $AgNO_3$(consumed) is of practically the same order as in the preceding experiment, but Ag : $AgNO_3$ and $AgNO_2$: $AgNO_3$, which are large at 130°, become small at 170°, increase, and remain fairly steady up to 240°: this shows that a nitrate-forming reaction becomes prominent after 130°; but expt. 1 has shown that it is prominent also at 130° in the first stages of the decomposition. The prominence at 130° is not likely to be due to nitrogen dioxide because its proportion is low in expt. 1 and higher in expt. 2—in the latter, nitrate formation has abated. Thus it appears that the cause of nitrate formation is different at 130° from that above 130°. In the latter case it may be due to dissociation of nitrogen dioxide (Richardson, *J.*, 1887, **51**, 397; Bodenstein and Kotayama, *Z. Electrochem.*, 1909, **15**, 244), producing oxygen as $NO_2 \rightleftharpoons NO + \frac{1}{2}O_2$. At and below 130°, however, it may be due to oxidation by silver oxide: $2AgNO_3 \rightleftharpoons Ag_2O + NO + NO_2$ (T. M. Oza and Shah, *J. Univ. Bombay*, 1942, **70**; T. M. Oza, *J. Indian Chem. Soc.*, 1945, **22**, 173; cf. Ostwald, *Annalen*, 1914, **403**, 32). The results show somewhat larger production of silver up to 2 hr. (expts. 1—3). With progress of the reaction and accumulation of nitrogen dioxide, silver may be used up as in (5) (Divers and Schimidzu, *loc. cit.*).

The above study makes it probable that nitrate formation occurs as $AgNO_2 + O = AgNO_3$, oxygen coming from silver oxide, $Ag_2O \rightleftharpoons 2Ag + O$ (Lewis, *Z. physikal. Chem.*, 1905, **52**, 310; *J. Amer. Chem. Soc.*, 1906, **28**, 139), at 130° and from dissociation of nitrogen dioxide above 130°. Silver oxide is known to decompose more readily in presence of nitric oxide (Auden and Fowler, *Chem. News*, 1895, **72**, 163; Sabatier and Senderens, *Compt. rend.*, 1892, **114**, 1429, 1476; **115**, 236). Silver nitrate is also reduced to nitrite by nitric oxide present in the system.

Decomposition of Mixtures of Silver Nitrite and Silver Oxide.—The results of decomposition of mixtures of silver nitrite (0·35 g.) with silver oxide (0·05 g.) are given in Table 2. Expts. 27—29 show the effect of time at 130° (cf. expts. 1—3, Table 1), and expts. 29—34 the effect of temperature in 2 hr. (cf. expts. 21—26, Table 1). At 130° the decomposition is retarded in the early stages, but this is not so at higher temperatures: some nitrogen is formed, more silver is formed, and yet neither the amount nor the proportion of nitrogen dioxide increases up to 1 hr. and silver nitrite consumed and nitrate formed are greater. In the later stages, the position is different: in 2 hr. nitrite consumed is less in expt. 29 than in expt. 3, though silver and silver nitrate formed continue to be greater in the former. As the temperature is 130° (<140°), increased formation of nitrate is probably not due to oxygen from nitrogen dioxide, and as a larger amount of silver is present, more silver oxide has decomposed; hence some silver nitrate in the 2-hr. experiment seems to have been formed from silver oxide as in (*a*) $Ag_2O + NO_2 = AgNO_2 + Ag$. In the earlier experiment, at 130°, however, the above data show that some nitrate may have been formed as in (*b*) $AgNO_2 + Ag_2O = AgNO_3 + 2Ag$.

TABLE 2. *Effect of time at* 130° *and of temperature on the decomposition of mixtures of silver nitrite* (0·35 *g.*) *with silver oxide* (0·05 *g.*) *for* 2 *hr.**

Expt. No.	Time (hr.)	Gas evolved (c.c. at N.T.P.) Total	NO	NO_2	N_2	Solid products : Ag	$AgNO_2$	$AgNO_3$ used	Ag_2O left (g.)	Ag / $AgNO_3$	Ag / $AgNO_2$	$AgNO_2$ / $AgNO_3$
27	½	2·58	1·54 (59·7)	1·04 (40·3)	nil	0·0167 (0·15)	0·0074 (0·044)	0·0242 (0·16)	0·0466	3·56	0·987	3·6
28	1	5·72	3·5 (60·8)	2·2 (39·1)	bubble	0·0362 (0·33)	0·0133 (0·078)	0·0464 (0·30)	0·0360	4·3	1·1	4·0
29	2	15·8	9·4 (59·4)	6·2 (39·5)	0·2 (1·1)	0·0692 (0·64)	0·0241 (0·14)	0·0857 (0·56)	0·0255	4·5	1·15	4·0
	Temp.											
30	170°	25·4	12·7 (49·8)	12·5 (49·1)	0·3 (1·1)	0·1256 (1·2)	0·0351 (0·21)	0·1619 (1·0)	0·0128	5·6	1·1	5·1
31	200	44·0	21·8 (49·6)	21·8 (49·6)	0·4 (0·8)	0·2091 (1·9)	0·0472 (0·28)	0·2714 (1·8)	nil	7·0	1·1	6·3
32	220	47·9	23·8 (49·6)	23·8 (49·6)	0·4 (0·8)	0·2254 (2·1)	0·0544 (0·32)	0·3013 (2·0)	nil	6·5	1·1	6·1
33	240	49·0	24·3 (49·6)	24·3 (49·6)	0·4 (0·8)	0·2408 (2·2)	0·0802 (0·47)	0·3458 (2·2)	nil	4·7	0·99	4·8
34	480	69·8	32·5 (46·6)	32·5 (46·6) (5·5)	0·9 (1·3)	0·2916 (2·7)	0·0033 (0·019)	0·3518 (2·3)	nil	139·2	1·2	120·5
			Plus O_2 = 3·9 c.c.									

* Parentheses are used as in Table 1.

The increased formation of nitrate in spite of the low nitrite consumption can arise also by the prevalence of the reaction (*c*) $Ag_2O + 2NO_2 = AgNO_3 + AgNO_2$, whereby nitrite may be replenished in the system. The behaviour of nitrogen dioxide towards silver oxide at 130° clarifies this point (see p. 2459).

At higher temperatures, the amount of nitrogen dioxide in the experiments of Table 2 is greater than in those of Table 1; that of silver formed is also greater, as expected; that of silver nitrate formed is also greater but those of silver nitrite consumed are identical. The last fact shows that either silver nitrite is replenished, as in eqn. (*c*), or silver nitrite is not consumed in making nitrate, as when nitrate is formed as in eqn. (*a*).

TABLE 3. *Effect of nitric oxide* (40 *cm. press.*) *on* Ag_2O (0·1 *g.*) *for different times at* 130° (*expts.* 35—37) *and at* 115° (38—43).*

Expt. No.	Duration (hr.)	Gas evolved (c.c. at N.T.P.) Total	NO_2	N_2	Solid products : Ag	$AgNO_2$	$AgNO_3$	Ag_2O used	Ag / Ag_2O	$AgNO_2$ / $AgNO_3$
35	½	0·76	0·59 (77·6)	0·17 (22·4)	0·0060 (0·055)	0·0039 (0·025)	0·0013 (0·0076)	0·0102 (0·044)	0·65	0·3
36	2	1·8	1·4 (80·3)	0·35 (19·6)	0·0159 (0·15)	0·0095 (0·062)	0·0032 (0·019)	0·0264 (0·11)	,,	,,
37	5	3·8	3·15 (83·8)	0·6 (16·2)	0·041 (0·38)	0·0219 (0·14)	0·0083 (0·049)	0·0662 (0·28)	,,	,,
38	½	0·4	0·25 (60·5)	0·15 (39·5)	0·0010 (0·0094)	nil —	test + —	0·0011 (0·0047)	1·0	—
39	2	1·2	0·7 (61·2)	0·5 (38·8)	0·0032 (0·030)	test + —	0·0021 (0·012)	0·0049 (0·021)	0·7	large
40	5	1·9	1·3 (67·5)	0·6 (32·5)	0·0051 (0·047)	0·0010 (0·0067)	0·0041 (0·024)	0·0092 (0·040)	0·6	3·6
41	10	3·9	2·8 (71·2)	1·1 (28·8)	0·0223 (0·21)	0·0104 (0·067)	0·00094 (0·055)	0·0383 (0·16)	0·6	0·8
42	15	6·0	4·2 (69·9)	1·8 (30·1)	0·0328 (0·30)	0·0219 (0·14)	0·0167 (0·098)	0·0633 (0·27)	0·5	0·7
43	20	7·3	5·1 (69·9)	2·2 (30·4)	0·0516 (0·48)	0·0388 (0·25)	0·0239 (0·14)	0·1010 (0·43)	0·5	0·56

* Parentheses are used as in Table 1.

Reaction of Silver Oxide and Nitric Oxide.—Experiments on the action of nitric oxide (under 40 cm.) on silver oxide (0·1 g.) are given in Table 3. Expts. 1—3 were done at 130° and 4—9 at 115°. The results show the presence of nitrogen dioxide, nitrogen, silver, silver nitrite, and silver nitrate. Nitrogen dioxide increases and nitrogen diminishes slowly with time. In

expts. 1—3 the quantities of nitrite are greater than those of nitrate; the ratios $\frac{1}{2}Ag : Ag_2O$(consumed) and $AgNO_3 : AgNO_2$ are both constant with time, showing the steady progress of the reaction with time: this shows that the reactions may be fairly rapid at 130°. Expts. 4—9 were therefore performed at 115°, and show that $\frac{1}{2}Ag : Ag_2O$ is about unity at the start and both this ratio and the ratio $AgNO_3 : AgNO_2$ diminish with progress of the reaction. No nitrite is present, and a test for nitrate (phenolsulphonic acid) is obtained after $\frac{1}{2}$ hr.; after 2 hr. nitrate is measurable but not nitrite; the quantities of both are measurable at the subsequent stages and the ratio $AgNO_3 : AgNO_2$ diminishes, showing that formation of silver nitrite increases with time more rapidly than that of the nitrate.

Since $\frac{1}{2}Ag : Ag_2O = 1$ at $\frac{1}{2}$ hr., the probable initial reaction is $Ag_2O = 2Ag + O$: this reaction is evidently induced by nitric oxide, for pure silver oxide scarcely began to decompose at 310°. The diminution in the value of this ratio with the progress of the experiment shows that this initial reaction is followed by reactions in which the oxide is so used as to liberate less silver metal, *i.e.*, by $Ag_2O + NO_2 = AgNO_3 + Ag$ or $Ag_2O_2 + 2NO_2 = 2AgNO_3$.

The fact that no nitrite is present in the initial stages when nitrate is indicated, shows that reactions like $Ag_2O + NO = AgNO_2 + Ag$ or $Ag_2O_2 + 2NO = 2AgNO_2$ may not occur and the formation of nitrite occurs as $AgNO_3 + NO = AgNO_2 + NO_2$ (Oza and Oza, *loc. cit.*).

Reaction of Nitric Oxide and Silver Nitrate at 128°.—Experiments on the action of nitric oxide (under 50 cm.) on silver nitrate (0·1 g.) at 115°, 120°, and 125° are given in Table 4. These

TABLE 4. *Effect of nitric oxide (50 cm. press.) on a fixed mass (ca. 0·1 g.) of silver nitrate at 115—125° for different times.*

Expt. No.	Temp.	Time (hr.)	$AgNO_3$ taken (g.)	Composition of gas (c.c.): Total	NO	NO_2	Residue (mg.) * $AgNO_2$	$AgNO_3$	$AgNO_3$ used
44	115—117°	6	0·1004	104·83	104·42	0·41	3·182	96·9	3·5
45	,,	12	0·1006	105·65	105·24	0·41	3·18	97·1	3·5
46	120—122	3	0·1026	111·23	110·24	1·09	7·4	94·4	8·2
47	,,	6	0·1024	106·78	105·15	1·63	11·15	90·1	12·3
48	,,	30	0·1006	107·09	105·46	1·63	11·15	88·3	12·3
49	125—127	3	0·1012	106·53	105·12	1·41	9·085	91·2	10·01
50	,,	6	0·1020	105·79	104·91	1·88	12·07	89·0	13·00
51	,,	12	0·1020	106·87	104·99	1·88	12·07	89·0	13·00

* No residue of Ag.

experiments were not performed at 130° since silver nitrite, an expected product of reaction, begins to decompose at 128° (see p. 2459). No silver is formed in these experiments; nitrogen dioxide is formed and its quantity remains unchanged after the equilibrium stage which, as the results show, is established in about 6 hr. These results therefore show that nitrite found in the experiments with silver oxide and nitric oxide is likely to have been formed by reduction of the nitrate by nitric oxide.

Reaction of Silver Oxide and Nitrogen Dioxide at 110°, 130°, *and* 250°. This reaction under our conditions has been studied in order to find out if the reaction $Ag_2O + 2NO_2 = AgNO_2 + AgNO_3$ occurs. The results of these experiments, each of which was done for $\frac{1}{2}$ hr., are given in Table 5 and show that the reaction produces both nitrite and nitrate but in a manner

TABLE 5. *Action of nitrogen dioxide on silver oxide at* 110—250°.

Expt. No.	Temp.	Ag_2O taken (g.)	N_2O_4 taken (g.) *	$AgNO_2$ formed (g.) †	$AgNO_3$ formed (g.) †	Ag formed (g.) †	Ag_2O left (g.) †	N_2O_3 formed (c.c.)	N_2O_4 left (c.c.)
52	110°	0·1040	0·2590 (63·0)	0·0114 (0·072)	0·0132 (0·078)	0·0110 (0·10)	0·0292 (0·125)	0·15	61·3
53	130	0·2630	0·2800 (68·2)	0·0616 (0·40)	0·0736 (0·434)	0·0972 (0·89)	0·201 (0·86)	nil	58·8
54	130	0·1086	0·3224 (78·5)	0·0123 (0·080)	0·01444 (0·085)	0·0117 (0·108)	0·0317 (0·13)	nil	—
55	250	0·1000	0·2912	0·00204	0·0559	0·05544	nil	0·25	67·1

* Parentheses give c.c.
† Moles or g.-atoms in parentheses.

that produces silver also. Little nitric oxide is liberated in the reaction, though there are indications that it is probably involved therein. The reactions may therefore be $Ag_2O + NO_2 = Ag_2O_2 + NO$ and $Ag_2O_2 + 2NO = 2AgNO_3$ (Addison and Lewis, *J.*, 1953, 1874) simultaneously with $Ag_2O + NO_2 = AgNO_3 + Ag$.

Reaction of Silver Nitrate with (a) *Nitrogen Dioxide and* (b) *Nitric Oxide.*—The course of reaction (*a*) at 120°, 130°, and 200° for ½ hr. is shown in Table 6. There is slight oxidation at 120° and at 130°, and a more distinct one at 200°; at 130° and 200°, silver is present, showing that nitrite has decomposed. The slight oxidation at 120° may be attributed to very slight dissociation of nitrogen dioxide below 140°, and presumably there is no oxidation by nitrogen dioxide (Addison

TABLE 6. *Action of nitrogen dioxide on silver nitrite at* 120°, 130°, *and* 200°.

Expt. No.	Temp.	$AgNO_2$ taken (g.)	N_2O_4 taken (g.)	$AgNO_2$ formed (g.)	Ag formed (g.)	$AgNO_2$ left (g.)	N_2O_4 formed (c.c.)	N_2O_4 left (c.c.)
56	120°	0·1010	0·2200	0·00894	nil	0·0929	1·6	52·1
57	130	0·2660	0·1480	0·0326	0·00432	0·2250	8·82	27·8
58	200	0·2060	0·2650	0·0916	0·0423	0·0625	12·00	56·88

and Lewis, *loc. cit.*) : the reaction is therefore $AgNO_2 + O = AgNO_3$. The reaction (*b*) for 2 hr. is shown in Table 7. There is slight production of nitrogen as may be expected (Oza, *loc. cit.*; Oza and Walawalker, *J. Indian Chem. Soc.*, **1945**, **22**, 243) because of absence of nitrate which permits the reaction $AgNO_2 + NO = AgNO_3 + \frac{1}{2}N_2$; the production of nitrate then represses this reaction as $AgNO_3 + NO \rightleftarrows AgNO_2 + NO_2$ is conspicuous as already observed.

TABLE 7. *Action of nitric oxide* (*press.* 50 *cm.*) *on* $AgNO_2$ (*fixed mass*) *for* 2 *hr. at* 130°, 150°, 170°, *and* 200°.

Expt. No.	Temp.	$AgNO_2$ taken (g.)	Gas in system at end (c.c.): Total	NO_2	NO	N_2	Residue (g.) : * $AgNO_2$	Ag (g.)	$AgNO_3$ (g.)	$AgNO_2$ used (g.) *
59	130°	0·3546	114·9	3·6	111·15	0·2	0·0349 (0·205)	0·0265 (0·245)	0·2834	0·07124 (0·463)
60	150	0·3534	120·4	5·4	114·45	0·5	0·0434 (0·255)	0·0530 (0·49)	0·2387	0·1147 (0·745)
61	170	0·3528	130·3	8·1	121·3	0·9	0·0514 (0·30)	0·0819 (0·76)	0·1893	0·1635 (1·06)
62	200	0·3500	142·6	12·2	129·3	1·1	0·0647 (0·38)	0·1018 (0·94)	0·1463	0·2037 (1·3)

* Parentheses used as in Table 1.

The above study has shown that under the conditions used in this work, of the possible solid products of the decomposition, *viz.*, silver and its nitrate and oxide, silver is likely to be slowly acted upon by nitrogen dioxide especially when the pressure in the system increases; nitrate is produced; silver nitrate reacts effectively with nitric oxide to replenish some of the consumed nitrite, and silver oxide reacts very effectively with nitric oxide even when the pressure of the gas is very small. An experiment showed that at 110—115° reaction occurred even when the pressure of nitric oxide was 5 cm. It thus became obvious that the cause of destruction of silver oxide lay probably in the simultaneous production of nitric oxide. If therefore nitric oxide

TABLE 8. *Decomposition of* $AgNO_2$ (*fixed mass*) *at* 130° *in oxygen* (11 *cm. press.*) *for varying periods* (a) *without addition of silver* (*expts.* 63—70) *and* (b) *with addition of finely divided silver* (*expts.* 71—74).*

Expt. No.	Time (hr.)	$AgNO_2$ taken (g.)	Gas in system at end (c.c.): Total	NO_2	N_2	O_2	Residue : Ag_2O (mg.)	Ag (mg.)	$AgNO_2$ (mg.)	$AgNO_3$ (mg.)	$AgNO_2$ used (g.)
63	¼	0·3510	110·1	1·1	nil	109·0	nil	1·62	328·0	23·0	23·0
64	½	0·3522	111·14	2·4	trace	108·7	nil	2·16	302·8	52·2	49·4
65	2	0·3522	108·4	3·00	0·11	105·3	nil	2·7	289·3	65·1	62·9
66	4	0·3506	108·3	4·2	0·15	104·0	1·32	3·2	269·8	82·2	80·8
67	6	0·3507	107·3	5·5	0·2	101·65	1·66	5·2	255·2	92·4	95·5
68	8	0·3546	107·3	6·0	0·22	101·0	1·5	6·7	241·9	111·2	112·7
69	10	0·3536	107·3	7·2	0·27	99·8	1·2	8·1	232·1	119·8	121·5
70	12	0·3538	105·9	9·2	0·20	96·6	1·2	10·8	216·7	122·1	137·1
71	½	0·3512	106·4	1·1	trace	105·3	nil	36·7	328·0	23·2	23·2
72	2	0·3504	106·7	2·8	0·14	103·8	nil	37·2	287·2	67·2	63·2
73	4	0·3522	107·4	4·2	0·18	103·0	1·28	38·4	270·5	83·7	81·7
74	8	0·3518	109·2	6·1	0·21	102·9	1·44	41·8	238·1	113·3	113·7

* Finely divided silver added in expts. 71—74 was, respectively, 0·0350, 0·0352, 0·0356, and 0·0352 g.

could be destroyed before it completely reacted with silver oxide, the latter might be isolated, at least in part.

Decomposition of Silver Nitrite in Oxygen at 130°.—The results of experiments with 0·35 g. of the nitrite decomposed for varying periods of time at 130° in an atmosphere of oxygen (11 cm. press.) are given in Table 8; they show the presence of silver oxide in the solid products after 4 hr. or more. Silver nitrite is present throughout along with its products of decomposition. It may be argued that the oxide may have been produced by the action of oxygen on finely divided silver produced in the system, but it must be remembered that silver nitrite is continuously decomposing and producing oxides of nitrogen so that the silver metal is in contact *not with oxygen* but with a mixture of nitrogen dioxide and oxygen: comparison with the results of time expts. (1—8, Table 1) shows that more nitrate is present in the experiments now described. Expts. 71—74 were done under the same conditions as expts. 1—8, but under oxygen and with the previous addition of 0·035 g. of silver to the 0·35 g. of nitrite: the results show larger formation of nitrate and no increased formation of silver oxide.

Conclusion.—The present study shows that the primary change in the decomposition of silver nitrite is

$$2AgNO_2 \rightleftharpoons Ag_2O + N_2O_3 (= NO + NO_2) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

This brings silver nitrite into line with the other nitrites already studied by Oza and his co-workers. The dissociation (1) is followed by reactions of silver oxide with nitric oxide (and also, to a certain extent, with nitrogen dioxide) to destroy the former. In the meanwhile some oxygen from silver oxide reacts with nitrite to form nitrate:

$$AgNO_2 + O = AgNO_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Nitrate, produced at higher temperatures, is produced from nitrite, and oxygen from nitrogen dioxide.

Silver oxide reacts vigorously with nitric oxide to produce nitrate as the primary product: nitrite is produced subsequently from the nitrate, thus replenishing nitrite:

$$AgNO_2 + NO \rightleftharpoons AgNO_3 + NO_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Silver oxide reacts with nitrogen dioxide to liberate silver and but little nitric oxide; the reaction may proceed by intermediate formation of silver peroxide:

$$Ag_2O + NO_2 = Ag_2O_2 + NO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

followed by the action of nitrogen oxide and dioxide on silver peroxide to produce nitrite and nitrate. Production of silver can be ascribed to the reaction

$$Ag_2O + NO_2 = AgNO_3 + Ag \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Nitrogen is never produced in the decomposition of silver nitrite, as nitrate is produced in the system almost from the start of the decomposition so that access of nitric oxide to nitrite is prevented by reaction (3).

Ultimately silver, silver nitrate, silver nitrite, nitric oxide, and nitrogen dioxide are left in the system except when the heating is intense (480°), in which case no nitrite is left. Neither silver nor silver nitrate appears to be the primary product of the reaction.

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The Self-condensation of Homophthalaldehyde.

By K. T. Potts and Sir Robert Robinson.

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A new view of the constitution of the product obtained by the action of hot aqueous sodium hydroxide on *iso*quinoline–sulphur trioxide is proposed and validated by the synthesis of the methyl-*o*-tolylnaphthalene of which the substance is the dioxo-derivative.

It is well known that hydrolytic fission of a pyridine nucleus provides derivatives of glutacondialdehyde (cf. " Heterocyclic Compounds," Ed. by Elderfield, Vol. I, p. 423, John Wiley and Sons Inc., New York). Thus the action of alkali on *iso*quinoline–sulphur trioxide should give homophthalaldehyde but Baumgarten and Olshausen (*Ber.*, 1931, **64**, 925) found that in fact the product was a phenylnaphthalenedialdehyde. Later (*Ber.*, 1935, **68**, 1316) Baumgarten showed that the same compound, $C_8H_{12}O_3$, could also be obtained in a similar manner from homophthalaldehyde prepared by the method of Blount and Robinson (*J.*, 1933, 555). The self-condensation thus disclosed was formulated as follows :

This is fully analogous to the condensation of phenylacetaldehyde to 2-phenylnaphthalene which, however, occurs under the influence of *acids*.

Although there are certain examples of ring-closure to a benzene ring which can be brought about by drastic methods using basic catalysts (*e.g.*, indoxyl from phenylglycine), it seemed to us that a more probable course of the reaction is that represented in the scheme :

(I)

On reduction by the Wolff–Kishner process, the dialdehyde gives a dimethylphenylnaphthalene and the synthesis of this substance has been effected with the result that the correctness of our view has been demonstrated.

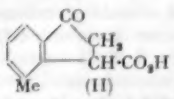
The first route attempted started with the Friedel–Crafts condensation of *o*-tolylsuccinic anhydride with benzene. Had this proceeded normally and similarly to the condensation of phenylsuccinic anhydride and veratrole (Robinson and Young, *J.*, 1935, 1414; cf. Rice, *J. Amer. Chem. Soc.*, 1931, **53**, 3159; Ali, Desai, Hunter, and Muhammed, *J.*, 1937, 1013) the later stages of the projected synthesis would probably have presented little difficulty. The product, under many conditions tried, was always 4-methylindan-1-one-3-carboxylic acid (II). This was decarboxylated in hot quinoline in the presence of copper bronze, to 4-methylindan-1-one (Young, *Ber.*, 1892, **25**, 2104).

The ultraviolet spectrum of the acid (II) was normal for the type, and the infrared spectrum showed absorption bands at 5·81 (unconjugated carboxyl), 5·94 (carbonyl in five-membered ring), and 12·75 μ (1 : 2 : 3-trisubstituted benzene).

The reaction between *o*-tolylsuccinic anhydride and phenylmagnesium bromide offered an alternative but this approach was unsuccessful.

o-Tolylideneacetophenone, prepared by an application of Weygand and Schächer's method (*Ber.*, 1935, **68**, 227), added hydrogen cyanide in the normal manner in the presence of acetic acid (cf. *Org. Synth.*, Coll. Vol., II, p. 498), yielding the nitrile (III; R = CN) which was then converted into the related amide (III; R = $CO{\cdot}NH_2$) and methyl ester (III; R = CO_2Me). The nitrile gave very poor yields of alcohol on reaction with methylmagnesium iodide, but the ester afforded a mixture of 4-phenyl-2-*o*-tolylpent-3-enoic acid

(IV) and the related γ-lactone (V); prolonged refluxing of the reaction mixture favoured the formation of the acid (cf. Kloetzel, *J. Amer. Chem. Soc.*, 1940, **62**, 1708). Both products were utilised; the acid (IV) was reduced catalytically (Adams), then cyclised to an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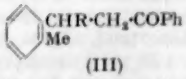
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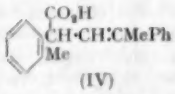
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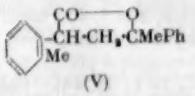
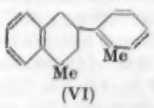
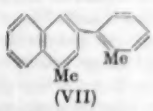
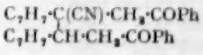

(V)

α-tetralone (anhydrous hydrofluoric acid) which was reduced to a tetralol (lithium aluminium hydride) and dehydrogenated (palladised charcoal) to the desired 1-methyl-3-*o*-tolylnaphthalene (VII). The lactone (V) was reduced, cyclised, and further reduced in one operation by heating with hydriodic acid, syrupy phosphoric acid, and red phosphorus (cf. Miescher and Billeter, *Helv. Chim. Acta*, 1939, **22**, 605; Dev, *J. Indian Chem. Soc.*, 1948, **25**, 323). The product was 1-methyl-3-*o*-tolyltetralin (VI) which was dehydrogenated to the naphthalene (VII) by means of palladised charcoal.


(VI)


(VII)


(VIII)

When *o*-tolylideneacetophenone was treated with potassium cyanide, the solution being alkaline, 3-cyano-1 : 6-diphenyl-3 : 4-di-*o*-tolylhexane-1 : 6-dione (VIII) was produced. It is assumed that initial formation of the normal adduct (III; R = CN) is followed by a Michael-type reaction with a second molecule of the unsaturated ketone; this process appears to be reversed when the substance is heated above its melting point.

The substance (VIII) shows no infrared absorption band which can be attributed to a cyano-group, whereas the nitrile (III; R = CN) showed both nitrile and carbonyl bands.

Dr. A. S. Bailey has kindly informed us that cyanodihydrosanguinarine also exhibits no nitrile absorption in the infrared region.

Experimental

Ultraviolet spectra were recorded in methanol, and evaporations were carried out under reduced pressure on the steam-bath.

*iso*Quinoline–*Sulphur Trioxide.*—The method of Baumgarten and Olshausen (*loc. cit.*) was used, the only variation being that the sulphonic acid was collected after about 5 min. to prevent any contamination by *iso*quinoline hydrochloride, which tended to separate when the solution was cooled for longer periods. The m. p. of an analytical specimen was 254—255° (lit., 250—254°) and tended to vary with the rate of heating (Found: C, 51·6; H, 3·7. Calc. for $C_9H_7O_3NS$: C, 51·6; H, 3·4%). Light absorption: $\lambda_{max.}$ 2300, 2650, 2750, 3320 (log ε 4·31, 3·29, 3·29, 3·64), $\lambda_{min.}$ 2500, 2700, 2950 (log ε 3·01, 3·28, 2·84).

2-Phenylnaphthalene-2′ : 4-dialdehyde (I).—*iso*Quinoline–sulphur trioxide (4·2 g.) was heated with an aqueous solution of sodium hydroxide (4·8 g. in 50 c.c.). The yellow solution soon became turbid and after 5 minutes' heating was cooled. 2-Phenylnaphthalene-2′ : 4-dialdehyde separated as needles (1·2 g.; m. p. 125—126°). It crystallised from aqueous methanol as needles, m. p. 126° (Baumgarten recorded m. p. 126·5° (Found: C, 82·7; H, 4·8. Calc. for $C_{18}H_{12}O_2$: C, 83·1; H, 4·7%). With concentrated sulphuric acid the aldehyde gave a yellow solution which became red when heated. It was insoluble in cold, concentrated nitric acid, and, on warming, a clear yellow solution was obtained. The di(phenylhydrazone), red needles from pentyl alcohol, had m. p. 198—200°, and the dioxime, white needles from aqueous alcohol, had m. p. 199°, in agreement with the values reported by Baumgarten.

1-Methyl-3-o-tolylnaphthalene (VII).—A mixture of 2-phenylnaphthalene-2′ : 4-dialdehyde (1·6 g.), ethylene glycol (30 c.c.), 90% hydrazine hydrate (6 c.c.), and sodium hydroxide (3 g.) was refluxed for 1 hr. and the temperature then raised to *ca.* 200° for a further hour. Water (50 c.c.) was added to the cooled solution and the product isolated by ether-extraction in the usual manner. *1-Methyl-3-o-tolylnaphthalene* distilled as a viscous oil, b. p. 118—120°/0·05 mm. (Found: C, 92·9; H, 6·8. $C_{18}H_{14}$ requires C, 93·1; H, 6·9%). The *1 : 3 : 5-trinitrobenzene*

complex was prepared in alcohol and it crystallised from methanol as yellow needles, m. p. 108—109° (Found : C, 54·8; H, 3·4; N, 12·8. $C_{15}H_{16},2C_6H_3O_6N_3$ requires C, 54·7; H, 3·4; N, 12·8%). The picrate was not suitable for purposes of characterisation.

o-Tolylsuccinic Acid.—In the preparation of α-cyano-*o*-methylcinnamic acid (cf. *Org. Synth.*, Coll. Vol. I, 2nd edn., pp. 181, 451) the yield was raised to about 74% when the amount of sodium hydroxide employed in the condensation was increased. The acid crystallised from water as hexagonal plates, m. p. 204—205° (Fiquet, *Ann. Chim.*, 1893, **29**, 484, gives m. p. 202°) (Found : C, 70·4; H, 4·8. Calc. for $C_{11}H_9O_3N$: C, 70·6; H, 4·8%). The ethyl ester was obtained in the usual way and crystallised from aqueous alcohol as large needles, m. p. 60° (*idem, loc. cit.*, reports m. p. 60°).

Ethyl αβ-dicyano-β-o-methyltolylpropionate can be hydrolysed to *o*-tolylsuccinic acid without further purification but a small amount was dissolved in ether and dried. It distilled as a slightly viscous oil, b. p. 155°/0·5 mm. (Found : C, 69·5; H, 6·0. $C_{14}H_{14}O_2N_2$ requires C, 69·4; H, 5·8%). *o*-Tolylsuccinic acid crystallised from water as small, irregular prisms, m. p. 181—182°, in agreement with Alder and Schmitz (*Annalen*, 1949, **565**, 99).

o-Tolylsuccinic Anhydride.—*o*-Tolylsuccinic acid (25 g.) was refluxed with pure, redistilled acetyl chloride (175 c.c.) for 2 hr., most of it had dissolved after 30 min. Excess of acetyl chloride and acetic acid was removed and the residue distilled as a very viscous oil (20·4 g., 90%), b. p. 145°/0·6 mm. On redistillation, *o-tolylsuccinic anhydride* was obtained as a viscous oil, b. p. 141°/0·5 mm. The anhydride crystallised after several months and was obtained as waxy prisms, m. p. 45—46°, by recrystallisation from ether (Found : C, 69·2; H, 5·3. $C_{11}H_{10}O_3$ requires C, 69·5; H, 5·3%). The *anilide*, readily obtained from the anhydride (300 mg.) and aniline (20 mg.) in benzene 8 c.c.), crystallised from aqueous methanol as needles, m. p. 167—168° (Found : C, 72·3; H, 6·0. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·1%).

7-Methyl-3-oxoindane-1-carboxylic Acid (II).—A mixture of *o*-tolylsuccinic anhydride (4·0 g.) and thiophen-free benzene (6·0 g.) was added to a solution of freshly sublimed aluminium chloride (7·5 g.) in nitrobenzene (20 c.c.) and kept in a stoppered flask for 48 hr. The complex was decomposed by ice and dilute hydrochloric acid, and the nitrobenzene and excess of benzene removed by steam-distillation. The remaining oil solidified; this was dissolved in sodium hydrogen carbonate solution and the solution extracted with ether. Acidification with dilute hydrochloric acid gave a partly crystalline precipitate (2·1 g., 50%; m. p. 154°). *7-Methyl-3-oxoindane-1-carboxylic acid* crystallised from benzene as irregular prisms, m. p. 157—158° (Found : C, 69·8, 69·6; H, 5·4, 5·5. $C_{11}H_{10}O_3$ requires C, 69·5; H, 5·3%). Light absorption : $\lambda_{max.}$ 2500, 2950 (log ε 4·04, 3·34), $\lambda_{min.}$ 2300, 2750 (log ε 3·62, 3·16). The acid gave positive reactions in the sodium nitroprusside–alkali and *m*-dinitrobenzene–alkali colour tests. With concentrated sulphuric acid it gave a yellow colour, becoming orange-red on warming and fading on dilution of the solution. The 2 : 4-*dinitrophenylhydrazone* crystallised from methanol as clusters of bright red needles, m. p. 259—260° (decomp.) (Found : C, 55·4; H, 3·7; N, 14·6. $C_{17}H_{14}O_6N_4$ requires C, 55·1; H, 3·8; N, 15·1%).

7-Methylindane-1-carboxylic Acid.—Amalgamated zinc was prepared by shaking zinc wool (1 g.), mercuric chloride (0·5 g.), concentrated hydrochloric acid (1 c.c.), and water (5 c.c.) for 5 min. and then decanting the solution. 7-Methyl-3-oxoindane-1-carboxylic acid (500 mg.), concentrated hydrochloric acid (2 c.c.), water (2 c.c.), and the amalgamated zinc were refluxed together for 8 hr. Concentrated hydrochloric acid (1 c.c.) was added at intervals of 3 hr. Overnight the oily product crystallised. *7-Methylindane-1-carboxylic acid* crystallised from water as glistening needles (450 mg.), m. p. 107° (Found : C, 75·2; H, 6·8. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·9%). The acid was soluble in most organic solvents and insoluble in water. It sublimed readily at atmospheric pressure and was slightly volatile in steam. Light absorption : $\lambda_{max.}$ 2100, 2650, 3200 (log ε 4·11, 2·68, 2·27), $\lambda_{min.}$ 2500, 2850 (log ε 2·49, 2·01).

4-Methylindan-1-one.—A mixture of 7-methyl-3-oxoindane-1-carboxylic acid (140 mg.), copper bronze (200 mg.), and quinoline (5 c.c.) was refluxed for 30 min. Ether was added to the cooled solution which was extracted with 10% hydrochloric acid, then with 2N-sodium hydroxide, washed with water, and dried (Na_2SO_4). Evaporation of the ether gave an oily residue which rapidly crystallised. 4-Methylindan-1-one separated from light petroleum as irregular prisms, m. p. 95—96° (Young, *Ber.*, 1892, **25**, 2104, reports m. p. 95°). It gave a positive reaction in the *m*-dinitrobenzene–alkali colour test. The phenylhydrazone crystallised from aqueous methanol as golden needles, m. p. 133° (*idem, loc. cit.*, reports m. p. 132°).

2-Methylstyryl Phenyl Ketone.—*o*-Tolualdehyde (2·0 g.; *Org. Synth.*, 1950, **30**, 99) was added to a mixture of acetophenone (2·0 g.), sodium hydroxide (0·5 g.), water (5 c.c.), and 95% ethanol (5 c.c.), and the whole shaken for 2 hr., during which an oil separated. After

24 hr. at 0°, an equal volume of water was added and the product isolated by means of ether. After a small forerun of acetophenone, 2-methylstyryl phenyl ketone distilled as a pale yellow, slightly viscous oil (3·4 g., 92%), b. p. 152°/0·5 mm. (Weygand and Schächer, *Ber.*, 1935, **68**, 227, give b. p. 218—219°/12 mm.). The 2 : 4-*dinitrophenylhydrazone* crystallised from methanol as orange needles, m. p. 167° (Found : C, 65·9; H, 4·4. $C_{23}H_{18}O_4N_4$ requires C, 65·7; H, 4·5%). The *semicarbazone* separated from aqueous methanol (charcoal) as white needles, m. p. 168° (Found : C, 72·9; H, 6·2. $C_{17}H_{17}ON_3$ requires C, 73·2; H, 6·1%).

β-*Benzoyl*-α-*o*-*tolylpropionitrile* (III; R = CN).—A solution of 2-methylstyryl phenyl ketone (4·4 g.) in 95% ethanol (70 c.c.) containing acetic acid (1·2 g.) was heated to 35° and then, with stirring, potassium cyanide (2·6 g.) in water (10 c.c.) was added. The stirring was continued for 3 hr. and, after standing overnight at 0°, the product (3·5 g., 73%; m. p. 84—85°) crystallised. The *nitrile* crystallised from 90% ethanol as needles, m. p. 89° (Found : C, 81·5; H, 6·3. $C_{17}H_{15}ON$ requires C, 81·9; H, 6·1%). The 2 : 4-*dinitrophenylhydrazone* crystallised from methanol as orange, irregular prisms, m. p. 163—164° (Found : C, 63·9; H, 4·4. $C_{23}H_{19}O_4N_8$ requires C, 64·3; H, 4·5%).

3-*Cyano*-1 : 6-*diphenyl*-3 : 4-*di*-*o*-*tolylhexane*-1 : 6-*dione* (VIII).—2-Methylstyryl phenyl ketone (3·3 g.) was treated with 50% ethanol (10 c.c.) and powdered sodium cyanide (1·5 g.). The oil did not completely dissolve and, after 30 min. on the steam-bath, became very viscous and partly solid. An equal volume of water was added, and, with cooling, an excess of concentrated hydrochloric acid. After decantation of the mother-liquor the resultant gum was dissolved in hot glacial acetic acid, and the product (0·7 g.; m. p. 241—242°) crystallised from the cooled solution. It separated from dilute acetic acid as rectangular plates, m. p. 246° (Found : C, 83·9; H, 6·4; N, 3·5. $C_{33}H_{29}O_2N$ requires C, 84·1; H, 6·2; N, 3·0%). It dissolved in concentrated sulphuric acid to an intense red solution. With concentated nitric acid a cherry-red colour was obtained.

β-*Benzoyl*-α-*o*-*tolylpropionamide*.—Concentrated sulphuric acid (10 c.c.) was added during 15 min. to a stirred suspension of β-benzoyl-α-*o*-tolylpropionitrile (10 g.) in glacial acetic acid (50 c.c.). After an hour at the room temperature, the deep red solution was poured on ice and next day the crystalline material (8·7 g., 82%; m. p. 159°) was collected. The *amide* crystallised from benzene as needles, m. p. 161° (Found : C, 76·2; H, 6·5. $C_{17}H_{17}NO_2$ requires C, 76·4; H, 6·4%).

Methyl β-*Benzoyl*-α-*o*-*tolylpropionate* (III; R = CO_2Me).—A mixture of β-benzoyl-α-*o*-tolylpropionamide (8·7 g.), ethanol (80 c.c.), and 2N-sodium hydroxide (80 c.c.) was refluxed until the evolution of ammonia ceased (10 hr.). Most of the alcohol was distilled off and water (50 c.c.) and excess of 3N-hydrochloric acid were added to the filtered liquid. The resultant gum was separated and dissolved in the minimum volume of methanol, and this solution treated with an excess of ethereal diazomethane. After 2 hr. at room temperature the solvent was removed and the residue crystallised from aqueous methanol. The *methyl ester* (4·5 g., 50%) separated from aqueous methanol as prisms, m. p. 90° (Found : C, 76·2; H, 6·4. $C_{18}H_{18}O_3$ requires C, 76·6; H, 6·4%). When the gum which separated after acidification of the reaction mixture was crystallised from glacial acetic acid needles of 4-*hydroxy*-4-*phenyl*-2-*o*-*tolylbut*-3-*enoic lactone* [2 : 3-*dihydro*-2-*oxo*-5-*phenyl*-3-*o*-*tolylfuran*], m. p. 248° (Found : C, 81·1; H, 5·8. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%), were obtained.

Reaction of Methyl β-*Benzoyl*-α-*o*-*tolylpropionate with Methylmagnesium Iodide*.—Methylmagnesium iodide (magnesium, 3·4 g.; methyl iodide, 19·6 g.) in ether (65 c.c.) was added with stirring to a solution of methyl β-benzoyl-α-*o*-tolylpropionate (28·2 g.) in ether (300 c.c.) at 0°. After being stirred for a further 30 min. at 0°, the mixture was allowed to reach the room temperature and then heated at 50—60° for 3 hr. During this period the precipitate formed a viscous, semi-solid mass. The complex was decomposed with ice and dilute hydrochloric acid, the ethereal layer was immediately separated, and the mother-liquor was extracted with a further quantity of ether (3 × 30 c.c.). After being shaken with sodium carbonate solution (3 × 20 c.c.) the extract was dried (Na_2SO_4) and evaporated, and the residual oil crystallised on the addition of a little methanol. δ-*Hydroxy*-δ-*phenyl*-α-*o*-*tolylvaleric lactone* (V) (5·0 g.) separated from methanol or light petroleum as beautiful needles, m. p. 120° (Found : C, 81·4; H, 6·9. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8%). A well-developed infrared band due to the carbonyl of the γ-lactone occurred at 5·64 μ. The sodium carbonate extract was decolorised by boiling with charcoal and, after cooling, was acidified with dilute hydrochloric acid. The oil which separated was isolated by means of ether in the usual manner and distilled as a pale yellow, very viscous oil (7·2 g.), b. p. *ca.* 200°/1 mm. 4-*Phenyl*-2-*o*-*tolylpent*-3-*enoic acid* (IV) crystallised from methanol as white needles, m. p. 117° (Found : C, 81·2; H, 6·9. $C_{18}H_{18}O_2$

requires C, 81·2; H, 6·7%). Esterification (diazomethane) gave *methyl* 4-*phenyl*-2-*o*-*tolylpent*-3-*enoate*, b. p. 145—147°/0·5 mm., n_D^{23} 1·6610 (Found: C, 81·5; H, 7·2. $C_{19}H_{20}O_2$ requires C, 81·4; H, 7·2%). A carbonyl band was present at 5·78 μ.

δ-*Phenyl*-α-*o*-*tolylvaleric Acid*.—A solution of the above unsaturated acid (5·0 g.) in methanol (30 c.c.) was shaken with hydrogen in the presence of Adams catalyst (0·8 g.) at room temperature and pressure. The theoretical volume of hydrogen (580 c.c.) was absorbed in 15 min. After isolation, the saturated *acid* distilled as a very viscous oil (4·4 g., 88%), b. p. 195°/1·5 mm. It crystallised from light petroleum as needles, m. p. 69—70° (Found: C, 80·5; H, 7·4. $C_{18}H_{20}O_2$ requires C, 80·5; H, 7·5%). With ethereal diazomethane it gave a *methyl ester*, b. p. 145° (bath-temp.)/1·5 mm., n_D^{23} 1·4260 (Found: C, 80·6; H, 7·9. $C_{19}H_{22}O_2$ requires C, 80·8; H, 7·9%).

1 : 2 : 3 : 4-*Tetrahydro*-4-*methyl*-1-*oxo*-2-*o*-*tolylnaphthalene*.—The foregoing acid (7·6 g.) was dissolved in anhydrous hydrogen fluoride (*ca.* 20 c.c.), and the copper vessel closed to the atmosphere. After 72 hr. the excess of hydrogen fluoride was removed in a stream of air on the steam-bath, the residue dissolved in ether, and the extract washed first with sodium carbonate solution and then with water. After drying and evaporation the viscous residue was distilled and the *tetralone* (3·6 g., 50%) obtained as a pale lemon-coloured, viscous oil, b. p. 147—150°/0·5 mm. (Found: C, 86·5; H, 7·3. $C_{18}H_{18}O$ requires C, 86·4; H, 7·3%). A prominent band (due to CO) was present at 5·95 μ. The 2 : 4-*dinitrophenylhydrazone* crystallised from acetone as orange-red needles, m. p. 279—280° (Found: C, 66·9; H, 4·8. $C_{24}H_{22}O_4N_4$ requires C, 67·0; H, 5·2%).

1 : 2 : 3 : 4-*Tetrahydro*-1-*hydroxy*-4-*methyl*-2-*o*-*tolylnaphthalene*.—The above tetralone (2·3 g.) in ether (40 c.c.) was added, slowly and with stirring, to a slurry of lithium aluminium hydride (3·5 g.) in ether (40 c.c.). After 30 minutes' stirring the excess of hydride was decomposed with dilute hydrochloric acid, and the ethereal layer separated, washed with water, and dried. The solution had an intense blue fluorescence in ultraviolet light. The *tetralol* distilled as a viscous fluorescent oil (1·5 g., 65%), b. p. 162°/0·5 mm. (Found: C, 85·8; H, 7·9. $C_{18}H_{20}O$ requires C, 85·7; H, 8·0%). Light absorption: $\lambda_{max.}$ 2040, 2550, 3800, 4200 (log ε 5·24, 4·46, 3·58, 3·56); $\lambda_{min.}$ 3700, 4000, 4200 (log ε 3·43, 3·47, 3·56). An absorption band was present at 2·96 μ (OH).

1 : 2 : 3 : 4-*Tetrahydro*-1-*methyl*-3-*o*-*tolylnaphthalene* (VI).—δ-Hydroxy-δ-phenyl-α-tolylvaleric lactone (4·1 g.), syrupy phosphoric acid (20 c.c.; *d*, 1·75), iodine (2·0 g.), and red phosphorus (4·0 g.) were heated together at 160—170° for 72 hr., then cooled, diluted with water, and extracted with ether. The extract was shaken with sodium carbonate solution (3 × 20 c.c.), washed with water, and dried (Na_2SO_4). After evaporation of the ether the *tetrahydronaphthalene* remained as a pale oil and distilled as a colourless, mobile oil (2·3 g., 64%) with a characteristic odour, b. p. 155°/1·5 mm., n_D^{23} 1·5880 (Found: C, 91·4; H, 8·5. $C_{18}H_{20}$ requires C, 91·5; H, 8·5%). The specimen for analysis was distilled from sodium.

1-*Methyl*-3-*o*-*tolylnaphthalene* (VII).—(*a*) 1 : 2 : 3 : 4-Tetrahydro-1-hydroxy-4-methyl-2-*o*-tolylnaphthalene (0·6 g.) was heated with palladised charcoal (0·5 g.) at 270—310° in a stream of nitrogen for 2 hr. The product, isolated by means of ether, was dissolved in alcohol, and 1 : 3 : 5-trinitrobenzene in alcohol added. The trinitrobenzene complex separated as yellow needles, m. p. 108°, alone and when mixed with a specimen prepared from the hydrocarbon obtained as above from the dialdehyde of Baumgarten and Olshausen (*loc. cit.*). The infrared spectra of the trinitrobenzene complexes were identical in all respects. (*b*) 1 : 2 : 3 : 4-Tetrahydro-1-methyl-3-*o*-tolylnaphthalene (0·7 g.) was heated with palladised charcoal (0·6 g.) at 270—310° in a stream of nitrogen for 2 hr. The product was isolated as the trinitrobenzene complex, m. p. 106—107°, raised to 108—109° on recrystallisation from methanol. The m. p. was not depressed on admixture with an authentic specimen of 1-methyl-3-*o*-tolylnaphthalene trinitrobenzene complex.

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Organic Peroxides. Part V. Isotopic Tracer Studies on the Formation and Decomposition of Organic Peroxides.*

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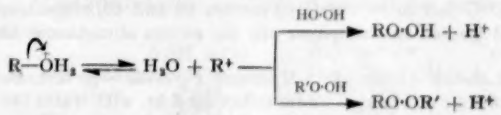
The formation of organic peroxides by the reaction of secondary and tertiary alcohols with hydrogen peroxide and with *tert.*-butyl hydroperoxide has been examined with the alcohols labelled with ^{18}O. Fission of the alkyl–oxygen bond of the alcohol is observed in all the reactions studied (cf. Davies *et al.*, Parts I and III *).

No ^{18}O exchange could be detected between $H_2{}^{18}O$ and hydrogen peroxide or 1-phenylethyl hydroperoxide under acid conditions, indicating again that an O–O bond was not formed by co-ordination of nucleophilic and electrophilic oxygen atoms. It is concluded that a synartetic mechanism may be involved in the O–O heterolysis of some organic peroxides.

In earlier papers * it was suggested that acid-catalysed reactions between secondary and tertiary alcohols, and hydrogen peroxide or alkyl hydroperoxides, are of S_N1 type, *i.e.*:



This conclusion was based on the following observations: (i) The reactivity of the alcohols (and their esters) could be correlated with their known or predicted readiness to undergo unimolecular alkyl–oxygen heterolysis. (ii) Optically active 1:2:3:4-tetrahydro-1-naphthol and 1-phenylethanol yielded the corresponding hydroperoxides with, respectively, racemisation, and racemisation accompanied by inversion, which is compatible with the formation of intermediate carbonium ions. (iii) Olefins could be caused to react with hydrogen peroxide and with *tert.*-butyl hydroperoxide in the presence of acid; in these reactions the intermediate carbonium ions are formed by protonation of the olefin (Davies and White, *Nature*, 1952, **170**, 668; Davies, Foster, and White, Parts I and III; Davies, Feld, and White, *Chem. and Ind.*, 1954, 1322).

This mechanism requires that both oxygen atoms in the peroxidic products should be derived from the hydrogen peroxide or alkyl hydroperoxide, and that the eliminated water should derive its oxygen from the alcohol. This has now been confirmed by the use of alcohols enriched in the ^{18}O isotope.

The ^{18}O was introduced into *tert.*-butanol, 1-phenylethanol, diphenylmethanol, 2-phenylpropan-2-ol, and triphenylmethanol, either by hydrolysis of the corresponding halide, or by acid-catalysed hydroxyl-exchange of the alcohol, with enriched water. These alcohols were then treated with acidified concentrated hydrogen peroxide, and the corresponding hydroperoxides were isolated by modifications of methods which we have described (Parts I and III); from the reaction of *tert.*-butanol with an equivalent amount of hydrogen peroxide, the water which was formed was also isolated. Similarly the reaction between triphenylmethanol and *tert.*-butyl hydroperoxide was carried out by the established method. The reactants and products were pyrolysed *in vacuo* and the abundance of the ^{18}O isotope was determined mass-spectrometrically.

Experimental

Materials.—Water enriched in ^{18}O was obtained by fractional distillation (Dostrovsky, Llewellyn, and Vromen, *J.*, 1952, 3509) and was chemically purified by distillation from alkaline permanganate.

* Parts I, II, III, IV, *J.*, 1953, 1541, 1808; 1954, 2200, 2204.

Hydrogen peroxide (99·5% and 87%) was supplied by Laporte Chemicals Limited, Luton.

2-Phenylpropan-2-ol (b. p. 93—94°/14 mm.) was prepared by the Grignard reaction between phenylmagnesium bromide and acetone.

Pyrolysis of Organic Compounds.—In preliminary experiments the decomposition of *tert.*-butanol and *tert.*-butyl hydroperoxide was carried out in sealed tubes at *ca.* 450° and 200° respectively. The water obtained from the alcohol was purified by static distillation and equilibrated with carbon dioxide; the carbon monoxide and dioxide obtained from the peroxide were analysed directly in the mass spectrometer.

It is possible that pyrolysis in a sealed tube at *ca.* 200° does not give accurate sampling of both the oxygen atoms of peroxides (*e.g.*, by formation of phenol as a primary decomposition product). This objection is eliminated in the following more general method which was applied to all the compounds which were studied. The organic compound was completely pyrolysed *in vacuo* to carbon monoxide, either on hot Monel gauze coated with carbon, or in a carbon tube heated by an induction furnace. The mass-spectrometric analysis was carried out directly on the carbon monoxide. The possible presence of atmospheric nitrogen (giving mass 28) was excluded by examining the samples for argon (mass 40).

Mass Spectrometric Analyses.—Mass-spectrometric analyses were carried out in a 180° mass spectrometer of conventional design. If R is the ratio $^{13}C^{16}O^{16}O : {}^{12}C^{16}O^{18}O$ for carbon dioxide and $^{13}C^{16}O : {}^{12}C^{18}O$ for carbon monoxide, the atoms % of ^{18}O (α') is given by: CO, $\alpha' = 100/(R + 1)$; CO_2, $\alpha' = 100/(2R + 1)$; H_2O, $\alpha' = 100/(2{\cdot}076R + 1)$ (Cohn and Urey, *J. Amer. Chem. Soc.*, 1938, **60**, 679; Dostrovsky and Klein, *Analyt. Chem.*, 1952, **24**, 414). The contributions of $^{13}C^{17}O$ and of $^{13}C^{16}O^{17}O$ to masses 30 and 46, respectively, were ignored. The atoms % excess (α) quoted in this paper are the excess abundances above those of the normal compounds.

The Reaction of ^{18}O-Labelled Alcohols with Hydrogen Peroxide.—(i) tert.-*Butyl alcohol. tert.*-Butyl chloride (20 c.c., 16·9 g.) was heated under reflux for 6 hr. with water (40 c.c.), α = *ca.* 0·5. Distillation yielded an azeotrope of the chloride, alcohol, and water. The aqueous layer was saturated with sodium chloride, and the upper layer separated, dried (K_2CO_3), and distilled, yielding *tert.*-butanol, b. p. 80—81°, which solidified on cooling.

A mixture of the above alcohol (3 c.c.), 87% hydrogen peroxide (3 c.c.), and sulphuric acid (0·03 c.c.) after 30 hr. at room temperature was extracted with light petroleum (3 c.c.), and the extract washed and dried (Na_2SO_4). Distillation yielded *tert.*-butyl hydroperoxide (1·39 g.), b. p. 37°/19 mm., which was redistilled, a middle fraction of 1·12 g. being collected at 32°/15 mm.

Both the water and *tert.*-butyl hydroperoxide were isolated from the reaction, in the following manner. After 15 days a mixture of 87% hydrogen peroxide (0·73 g.), concentrated sulphuric acid (0·010 g.), and *tert.*-butanol (1·3 g., 1 mol.), was still homogeneous but smelled strongly of *tert.*-butyl hydroperoxide. On the addition of light petroleum (5 c.c.) a lower layer of water was formed, which was separated and washed three times with light petroleum. The combined petroleum extracts were distilled, yielding *tert.*-butyl hydroperoxide (0·53 g.), b. p. 40—41°/13 mm.

(ii) 1-*Phenylethanol.*—A mixture of 1-phenylethyl chloride (10 c.c., b. p. 88°/25 mm.) was shaken with ^{18}O-enriched water (100 c.c.) at 50° for 12 hr. The organic layer was separated, washed with aqueous sodium carbonate, and dried (Na_2SO_4). Distillation yielded 1-phenylethanol (4 c.c.), b. p. 102—104°/18 mm., n_D^{25} 1·5246.

A mixture of this alcohol (3 c.c.), hydrogen peroxide (8 c.c.), and concentrated sulphuric acid (0·05 c.c.) was shaken for 2 hr. at 0° and 4 hr. at room temperature. Water (20 c.c.) was added and the product extracted with ether, washed with aqueous sodium hydrogen carbonate and with water, and dried (Na_2SO_4). Distillation yielded 1-phenylethyl hydroperoxide, b. p. 46°/0·2 mm., n_D^{25} 1·5230.

(iii) *Diphenylmethanol.* A 6% solution of diphenylmethanol in dioxan–$H_2{}^{18}O$ (70 : 30 v/v) which was 0·06N with respect to hydrogen chloride, was kept at 100° for 2 hr. The solvent was removed in a high vacuum, giving diphenylmethanol, m. p. 67—68° after recrystallisation from light petroleum. We are indebted to Mr. R. H. Flowers for carrying out this reaction.

The alcohol (1·0 g.), in the minimum of ether, was stirred with 87% hydrogen peroxide (10 c.c.) and concentrated sulphuric acid (0·02 c.c.) at 0° for 5 hr. By the usual procedure, diphenylmethyl hydroperoxide was isolated (from light petroleum; 0·43 g.), m. p. and mixed m. p. 50—52·5°, liquid when ground with benzophenone.

(iv) 2-*Phenylpropan*-2-*ol.* 2-Phenylpropan-2-ol (10 c.c.; b. p. 94—95°/13 mm.) was shaken with ^{18}O-enriched water (9·5 c.c.; α = *ca.* 2·8%) and sulphuric acid (0·5 c.c.) for 48 hr. at room temperature. The alcohol was recovered (b. p. 93—94°/13 mm.).

The alcohol (2·7 c.c.) was shaken with 87% hydrogen peroxide (8 c.c.) containing sulphuric acid (0·05 c.c.) at 0° for 2 hr. and at room temperature for 4 hr. Isolation of the product in the usual manner yielded 1-methyl-1-phenylethyl hydroperoxide; on distillation at 70°/0·4 mm. some decomposition occurred, the odour of phenol being present in the product which had a high refractive index, n_D^{20} 1·5319 (literature, n_D^{20} 1·5242). This partial decomposition, however, should not invalidate the result of the mass-spectrometric measurement.

(v) *Triphenylmethanol.* A sample of triphenylmethanol (m. p. 160—161°) enriched in ^{18}O was kindly provided by Dr. J. R. Quayle.

The finely powdered alcohol (2·0 g.) was added to 83% hydrogen peroxide (5 c.c.) containing concentrated sulphuric acid (0·05 c.c.). Sufficient ether was added from time to time to dissolve the triphenylmethanol. After 9 hours' stirring, and 18 hours' storage, the ether was allowed to evaporate, yielding a solid (2·0 g.; m. p. 79—80°) which was filtered off. Recrystallisation from ether–light petroleum gave triphenylmethyl hydroperoxide (0·99 g.), m. p. 83—86° (Found: C, 82·7; H, 6·2. Calc. for $C_{19}H_{16}O_2$: C, 82·6; H, 5·8%).

The Reaction of ^{18}O*-labelled Triphenylmethanol with* tert.*-Butyl Hydroperoxide.*—*tert.*-Butyl hydroperoxide (0·5 g.) was added to a solution of the above triphenylmethanol (1·3 g.) in glacial acetic acid (29 c.c.); on the addition of sulphuric acid (0·06 c.c.) a yellow colour developed. After 4 hr. the pale yellow solution was poured on ice, and the precipitated solid was twice recrystallised from methanol, yielding *tert.*-butyl triphenylmethyl peroxide (0·91 g.), m. p. 72·5—73°.

Mass-spectrometric analyses of alcohols and peroxides.

Alcohol	α	Peroxide	α
$Me_3C{\cdot}OH$	0·501, 0·510	$Me_3C{\cdot}O{\cdot}OH$ [b]	0·007, 0·005,[a] 0·010 [a]
$Ph{\cdot}CHMe{\cdot}OH$	0·765	$Ph{\cdot}CHMe{\cdot}O{\cdot}OH$	0·007
$Ph_2CH{\cdot}OH$	0·354	$Ph_2CH{\cdot}O{\cdot}OH$	0·001
$Ph{\cdot}CMe_2{\cdot}OH$	1·87	$Ph{\cdot}CMe_2{\cdot}O{\cdot}OH$	0·019
$Ph_3C{\cdot}OH$	0·407	$Ph_3C{\cdot}O{\cdot}OH$	0·000
,,	,,	$Ph_3C{\cdot}O{\cdot}O{\cdot}CMe_3$	0·002, 0·002 [a]

[a] By pyrolysis in a sealed tube. [b] The water which was isolated from the reaction between equivalents of *tert.*-butanol and 87% hydrogen peroxide had α = 0·389. If allowance is made for dilution by the 13% of normal water initially present in the hydrogen peroxide, the water liberated by the alcohol should have α = 0·392.

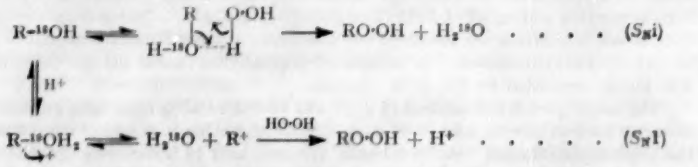
The Absence of Oxygen Exchange between Hydrogen Peroxide and Water.—99·5% Hydrogen peroxide (18·015 g.) was mixed with water (2·620 g.) enriched in ^{18}O (α 9·1), giving 87·4% aqueous hydrogen peroxide. Part of this mixture (0·620 g.) was acidified with 0·02 g. of sulphuric acid. After 14 hr. at room temperature, half the reaction mixture (sample *a*) was separated and stored at −80°; the second half was similarly treated after 7 days (sample *b*). Two drops of each sample were then decomposed with an excess of acidified potassium permanganate in a Y-tube, and the oxygen which was evolved was analysed mass-spectrometrically and compared with that from an 87% solution of hydrogen peroxide in normal water: (*a*) α = 0·001; (*b*) α = 0·001. It has been shown (Bunton and Llewellyn, *Research*, 1952, **5**, 142; Cahill and Taube, *J. Amer. Chem. Soc.*, 1952, **74**, 2312; Dole, Rudd, Muchow, and Comte, *J. Chem. Phys.*, 1952, **20**, 961) that the oxygen evolved in this reaction is derived wholly from the hydrogen peroxide.

The Absence of Oxygen Exchange between 1*-Phenylethyl Hydroperoxide and Water.*—A mixture of 1-phenylethyl hydroperoxide (1·0 c.c.), ^{18}O-enriched water (9·0 c.c.) (α 2·8), and sulphuric acid (1·0 c.c.) was shaken for 3 hr. After 3 days, the discoloured upper layer was extracted with ether, washed with aqueous sodium hydrogen carbonate and with water, and dried (Na_2SO_4). The ether was removed at the pump and the majority of the phenol by sublimation on to a cold finger. By the usual procedure (Part III) the 1-phenylethyl hydroperoxide was isolated from residual phenol by the formation of 1-phenylethyl triphenylmethyl peroxide, m. p. 84°, α 0·006. The results recorded earlier in this paper, and work on the triphenylmethylation of optically active 1-phenylethyl hydroperoxide (Davies, Feld, and White, *loc. cit.*), demonstrate that the peroxide bond remains intact during the alkylation.

Discussion

The results recorded in the Table demonstrate unequivocally that the oxidation of the alcohols proceeds by alkyl–oxygen fission, and to that limit confirm our conclusion that alkyl–oxygen heterolysis occurs, principally by a unimolecular mechanism. Recent

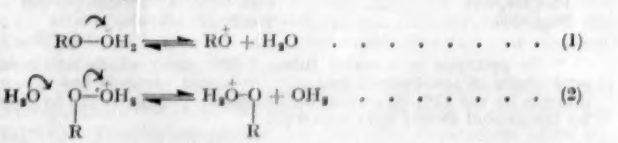
results which we have obtained on the reactions of optically active alcohols (Davies and Feld, unpublished work) indicate that the S_N1 mechanism may sometimes be accompanied by an S_Ni component, *i.e.*:



The possibility of any major portion of the reaction proceeding by electrophilic attack of $H_2\overset{+}{O}$–OH or of $\overset{+}{O}$H on the oxygen atom of the alcohol (or by attack of $H_2\overset{+}{O}$–OBu^t or of $\overset{+}{O}$–Bu^t in the reaction of *tert.*-butyl hydroperoxide with triphenylmethanol) is excluded.

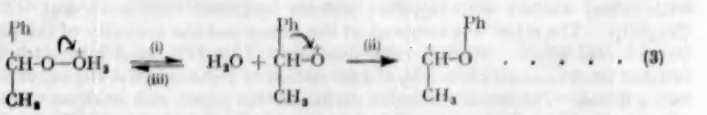
Further attempts to detect this acid-catalysed formation of an O–O bond by the co-ordination of electrophilic and nucleophilic oxygen were made in the following two experiments using more highly ^{18}O-enriched water.

87·4% Hydrogen peroxide containing water with 9·1% excess of ^{18}O was acidified with sulphuric acid; no exchange of oxygen between the hydrogen peroxide and water could be detected after 7 days. The equilibria (1) and (2) (R = H), which involve respectively S_N1 and S_N2 reaction at an oxygen atom, do not therefore exist under these conditions. This result confirms and extends those obtained earlier on dilute aqueous acidic solutions of hydrogen peroxide (Bunton and Llewellyn, *loc. cit.*).



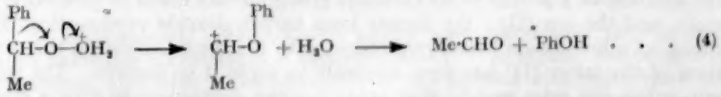
A similar experiment was conducted with 1-phenylethyl hydroperoxide in which heterolysis of the O–O bond might again proceed by an S_N1 or S_N2 mechanism [equations (1) and (2), R = Ph·CHMe–], both of which would involve oxygen exchange with added water. The hydroperoxide was treated with ^{18}O-enriched water and sulphuric acid so that partial decomposition to phenol occurred. The undecomposed hydroperoxide, which was isolated as its triphenylmethyl derivative, contained oxygen of approximately normal isotopic constitution. Again, therefore, under these experimental conditions, there is no evidence for the formation of a peroxide link by the co-ordination of electrophilic and nucleophilic oxygen.

This result also provides evidence of the mechanism of the ready acid-catalysed rearrangement of the hydroperoxide to form phenol and acetaldehyde (Kharasch, Fono, and Nudenberg, *J. Org. Chem.*, 1951, **16**, 128). The two processes involved—removal of water (i) and migration of a phenyl group (ii)—may occur stepwise (equation **3**) or by a synchronous mechanism.



The absence of ^{18}O-exchange in 1-phenylethyl hydroperoxide during decomposition shows either that the rate of migration of the phenyl group (ii) is very much greater than the rate of reaction of the alkoxy-cation with water (iii), or that steps (i) and (ii) are not distinct but combine to form a single step. The latter mechanism implies synartetic acceleration of the rearrangement, and it would be difficult to account for the high rate of acid-catalysed decomposition of 1-phenylethyl hydroperoxide compared with that of *tert.*-butyl hydroperoxide except on this assumption. It appears that the migrating phenyl

group assists in the heterolysis of the O–O bond (equation 4), the reaction being analogous to the ready unimolecular solvolysis with rearrangement of 2 : 2 : 2-triphenylethyl chloride (Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 514).



The authors are indebted to Professors E. D. Hughes, F.R.S., and C. K. Ingold, F.R.S., for their interest. Grateful acknowledgment is made to Messrs. Laporte Chemicals Limited for the gift of hydrogen peroxide and *tert.*-butyl hydroperoxide, and to the Society of Chemical Industry for the award of the John Gray Jubilee Scholarship (to M. B.).

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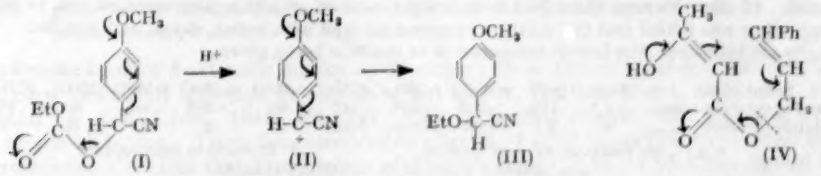
The Decarboxylation of Some α-Ethoxycarbonyloxybenzyl Cyanides.

By JOHN A. D. JEFFREYS.

[Reprint Order No. 6109.]

α-Ethoxycarbonyloxybenzyl cyanides with an electron-releasing group in the *ortho*- or *para*-position lose carbon dioxide on being heated with a catalytic quantity of sulphuric acid; if the electron-releasing group is very active, the α-ethoxybenzyl cyanide is formed.

α-ETHOXYCARBONYLOXY-*p*-METHOXYBENZYL CYANIDE (I) was readily decarboxylated in the presence of a trace of sulphuric acid at 80° to the ether (III), and the *o*-methoxy-isomer reacted similarly but more slowly; the ester derived from furfuraldehyde cyanohydrin was sufficiently activated by the heterocyclic oxygen atom to be decarboxylated but the resulting ion was too unstable to survive. The electron-releasing capacity of a methyl group or chlorine atom is less than that of a methoxyl group, and this is reflected in the higher temperature necessary to effect decarboxylation of the esters with these *para*-substituents, and in the instability of the resulting ions. The esters derived from the cyanohydrins of *p*-tolualdehyde and *p*-chlorobenzaldehyde were decarboxylated, but gave only polymeric material. Esters having no *ortho* or *para* electron-releasing substituents did not lose carbon dioxide, and could, in some cases, be recovered to some extent.



The reaction falls into the class of alkyl–oxygen ester fission (see Kenyon *et al.*, *J.*, 1942, 556, 605; 1946, 797, 803, 807; 1951, 376, 380, 382, 385, 386; 1952, 4964; 1953, 3619; 1954, 779, 3474) and requires the same electronic displacements. Related reactions are the acid-catalysed decomposition of the acetoacetates of tertiary ethynylmethanols and *tert.*-butanol, and the pyrolysis of the β-keto-esters of allyl alcohols (see Lacey, *J.*, 1954, 827).

The decomposition of cinnamyl acetoacetate to 1-methyl-2-phenylbut-3-en-1-one (Kimel and Cope, *J. Amer. Chem. Soc.*, 1943, **65**, 1992) is interesting, as the enolate, (IV), *i.e.*, the reacting species, is in some measure a bisvinylogue of the systems described in this paper (*e.g.*, I). The low temperature needed for the reaction recalls the acid-catalysed pyrolysis of β-keto-esters of *tert.*-butanol, the inductive effect of the three methyl groups

being replaced by the tautomeric effect of, for example, a methoxyl group. However, the initially formed benzyl cation cannot lose a proton to give an olefin, but must either recombine with a negative ion to give, in this case, an ether, or decompose. Thus the ester, after addition of a proton to its carbonyl group, breaks down to give ethyl hydrogen carbonate, and the ion (II); the former loses carbon dioxide regenerating the proton, and forming an ethoxide ion which recombines with the benzyl cation, if the resonance stabilisation of the latter (II) has been adequate to allow it to survive. The reaction will not occur unless the ester moiety that separates can decompose to give a strong base; the benzoyl and *p*-methoxybenzoyl derivatives of *p*-methoxymandelonitrile (Francis and Davies, *J.*, 1904, **1404**) were refluxed in benzene with a trace of sulphuric acid. Extensive decomposition occurred in both cases, but no carbon dioxide was evolved; in the latter case a small quantity of anisic acid was isolated as the sole crystalline product.

Experimental.

Unless stated otherwise, the light petroleum had b. p. 40—60°.

α-Ethoxycarbonyloxybenzyl Cyanides.—These were prepared by Kindler's method (*Arch. Pharm.*, 1950, **283**, 190) and distilled *in vacuo*. All except those marked * decomposed to some extent on distillation.

				Found (%)				Required (%)			
Subst.	B. p./mm.	n_D^{21}	Formula	C	H	N	Cl	C	H	N	Cl
*None [1]	110°/0·5	1·4972	$C_{11}H_{11}O_3N$	64·7	5·2	6·8	—	64·4	5·4	6·8	—
**p*-Cl	124/0·4	1·5131	$C_{11}H_{10}O_3NCl$	55·2	4·4	6·0	14·9	55·1	4·2	5·9	14·8
m-NO_2 [2]	160/0·4	(1·5272/17)	$C_{11}H_{10}O_5N_2$	53·1	4·2	11·2	—	52·8	4·0	11·2	—
p-NO_2	158/0·4	1·5265	$C_{11}H_{10}O_5N_2$	53·0	4·0	11·0	—	52·8	4·0	11·2	—
p-Me	121/0·6	1·4990	$C_{12}H_{13}O_3N$	66·0	6·1	6·7	—	65·8	5·9	6·4	—
o-MeO.....	136/0·6	1·5061	$C_{12}H_{13}O_4N$	61·8	5·4	6·2	—	61·3	5·5	6·0	—
**m*-MeO ...	132/0·4	1·5048	$C_{12}H_{13}O_4N$	61·3	5·4	5·8	—	61·3	5·5	6·0	—
p-MeO [3]	128/0·25	1·5100	—	—	—	—	—	—	—	—	—
3 : 4-$(MeO)_2$	Decomp.	—	—	—	—	—	—	—	—	—	—
3 : 4-(CH_2O_2)	156/0·4	1·5208	$C_{12}H_{11}O_5N$	57·9	4·6	5·9	—	57·8	4·4	5·6	—

[1] Francis and Davies (*loc. cit.*) gave a poor analysis. [2] Subsequently solidified, plates from MeOH, m. p. 60—61°. [3] Buck (*J. Amer. Chem. Soc.*, 1933, **55**, 2593).

α-Ethoxycarbonyloxyfurfuryl Cyanide.—This nitrile was also prepared by Kindler's method; it had b. p. 94°/0·5 mm., n_D^{21} 1·5208 (cf. Lukes, Kastner, and Herben, *Coll. Czech. Chem. Comm.*, 1947, **12**, 647).

Acetophenone gave no nitrile by this method and was recovered.

α-Ethoxybenzyl Cyanides.—The ethoxycarbonyloxy-cyanide was refluxed with 5 times its volume of solvent (benzene, b. p. 80°; toluene, b. p. 110°; xylene, b. p. 140°; or tetralin, b. p. 206°) containing 2 drops of concentrated sulphuric acid, till evolution of carbon dioxide ceased. If after 10 min. there had been no gas evolved, reaction was assumed not to occur. Much ether was added and the mixture was washed well with water, dried, and distilled. The results are tabulated, the lowest temperature of reaction being given.

Substituent	None	*p*-Cl	*m*-NO_2	*p*-NO_2	*p*-Me	*o*-MeO	*m*-MeO	*p*-MeO	3 : 4-$(MeO)_2$	3 : 4-(CH_2O_2)
Decarboxylation temp.	n.r.*	110	>206	>206	140	80	>206	80	80	80
Volatile product	S	S†	None	None	None	E	S	E	E	E

* n.r.—no reaction, even in tetralin. † If reaction interrupted.
S = Starting material, E = ethoxy-cyanide.

When α-ethoxycarbonyloxyfurfuryl cyanide was treated in the same way at 80° no volatile product was obtained.

The properties of *α-ethoxybenzyl cyanides* are tabulated below.

				Found (%)			Reqd. (%)			
Substituent	B. p./mm.	n_D^{21}	Formula	C	H	N	C	H	N	Yield †
o-MeO	110°/0·8	1·5100	$C_{11}H_{13}O_2N$	69·0	6·6	7·5	69·1	6·8	7·3	16% ‡
p-MeO *	110/0·5	—	$C_{11}H_{13}O_2N$	69·3	7·2	7·5	69·1	6·8	7·3	41 §
3 : 4-$(MeO)_2$ ...	136/0·6	1·5233	$C_{12}H_{15}O_3N$	65·3	6·9	6·2	65·2	6·8	6·3	60 §
3 : 4-(CH_2O_2) ...	142/0·6	1·5213	$C_{11}H_{11}O_3N$	64·5	5·3	7·1	64·4	5·4	6·8	61 §

* n_D^{21} 1·5118; subsequently solidified, forming needles, m. p. 27°, from light petroleum.
† On initial aldehyde. ‡ 66% on ester. § Without isolation of intermediate ester.

These were colourless liquids, except for the 3 : 4-dimethoxy-compound; in this decarboxylation a yellow material was produced (needles from dioxan, m. p. 300°) which sublimed readily (180°/0·4 mm.), and coloured the distillate slightly. Solutions of this solid had an intense blue fluorescence (Found: C, 68·4; H, 5·5; N, 8·1. $C_{20}H_{20}O_4N_2$ requires C, 68·2; H, 5·7; N, 7·9%).

Hydrolysis of the α-Ethoxybenzyl cyanides.—The nitriles were boiled with 10% aqueous-ethanolic potassium hydroxide till evolution of ammonia ceased. The ethanol was evaporated off, and the liquid washed with ether. The aqueous layer was acidified with hydrochloric acid and extracted with ether. This extract was shaken with sodium carbonate solution, and the aqueous layer was reacidified and extracted with ether. Evaporation of the dried extract left a brownish oil which was extracted with light petroleum to yield the corresponding *acids*; the 3 : 4-methylenedioxy-acid was dimorphic. Their properties, together with those of the corresponding *amides* (obtained *via* the acid chlorides) are tabulated below.

Substituent	Description	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Reqd. (%) C	Reqd. (%) H	Reqd. (%) N
			Acids						
o-MeO	Tablets from benzene–petrol ...	48°	$C_{11}H_{14}O_4$	63·0	6·6	—	62·8	6·7	—
p-MeO	Oil, decomposing on attempted distillation	—	—	—	—	—	—	—	—
3 : 4-$(MeO)_2$...	Prisms from CCl_4–petrol	86	$C_{12}H_{16}O_5$	59·9	6·5	—	60·0	6·7	—
3 : 4-(CH_2O_2)	(*a*) Tablets from CCl_4–petrol ...	68	$C_{11}H_{12}O_4$	58·9	5·2	—	58·9	5·4	—
	(*b*) Needles from CCl_4–petrol ...	76	$C_{11}H_{12}O_5$	59·0	5·4	—	58·9	5·4	—
			Amides						
o-MeO	Rhombs and plates from benzene	110—111°	$C_{11}H_{15}O_3N$	63·2	6·9	7·0	63·1	7·2	6·7
p-MeO	Needles from benzene	120	$C_{11}H_{15}O_3N$	63·3	7·0	6·5	63·1	7·2	6·7
3 : 4-$(MeO)_2$...	Needles from benzene	107	$C_{12}H_{17}O_4N$	60·1	7·1	6·0	60·3	7·1	5·9
3 : 4-(CH_2O_2)	Plates from petrol (b. p. 60—80°)	102	$C_{11}H_{13}O_4N$	59·4	5·5	6·2	59·2	5·8	6·0

The author is grateful to Mr. J. M. L. Cameron and his assistants for the microanalyses.

GLASGOW UNIVERSITY. [*Received, February 8th*, 1955.]

Studies in the Steroid Series. Part LXIX. Bromination of 11-Oxo-5α-steroids.*

By H. B. HENBEST, E. R. H. JONES, A. A. WAGLAND, and T. I. WRIGLEY.

[Reprint Order No. 6139.]

Bromination of an 11-oxo-5α-steroid gave a 9α-bromo-ketone in high yield. This was converted into a Δ^8-11-ketone with collidine, and somewhat unexpectedly by lithium aluminium hydride into the 9β : 11β-epoxide and by sodium borohydride into the original ketone.

THE bromination of 5α-steroids having an 11-oxo-group as the only ketonic function has not been described, although in the 5β-series Turner, Mattox, Engel, McKenzie, and Kendall (*J. Biol. Chem.*, **1946**, **166**, 345; **1948**, **173**, 283) reported the isolation of a 12α-bromo-11-ketone. From the considerable amount of work on cortical compounds and intermediates it is clear that bromination of 11-ketones of the 5α- or 5β-series cannot be too rapid as halogenation adjacent to other ketonic functions (*e.g.*, 3-oxo and/or 20-oxo) always occurs preferentially. In view of current interest in routes to 9-halogeno-steroids, the bromination of the simpler system, 3β-acetoxyergostan-11-one (I), has been studied.

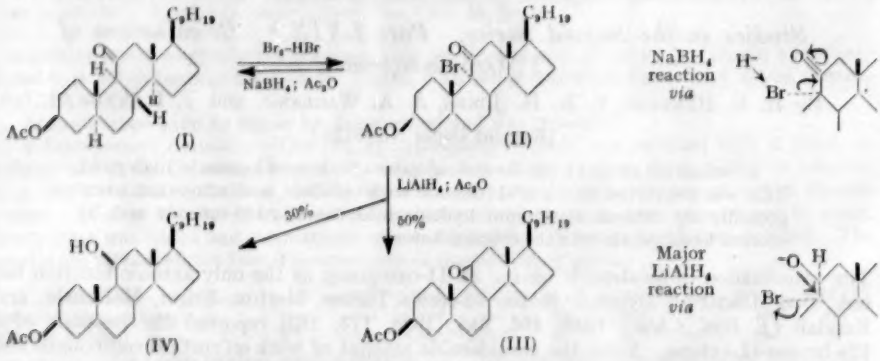
This ketone in acetic acid at room temperature was treated with bromine (1 mol.) in the presence of hydrogen bromide, the solution being decolourized in 30—60 minutes. Isolation in the usual way gave a high yield of bromo-ketone [shown to be (II), see below]. However, on some occasions, although the bromination proceeded at about the same rate, a mixture was produced. It was considered possible that this occasional erratic course might be due to the adventitious presence or absence of substances promoting a free-radical reaction, for Kharasch, Sternfeld, and Mayo (*J. Amer. Chem. Soc.*, **1937**, **59**, 1655)

* Part LXVIII, *J.*, 1955, 2176.

have reported that the isomerization of a bromo-ketone may be accelerated by peroxides, oxygen, or illumination. Bromination of (I) in the dark in air, in daylight in nitrogen, or in the dark in nitrogen (one experiment each) led in each case to good yields of the bromo-ketone, the rate of bromination not being appreciably altered. Finally it was found that bromination at 40° in the dark in nitrogen gave 85% yields of bromo-ketone (3 experiments), the reaction being complete in less than 5 minutes. Although further experimentation is necessary to determine more precisely the factors causing the occasional formation of mixtures in the earlier experiments, it seems likely that still closer attention to reaction conditions may often be of value in the bromination of ketones.

The major product of sodium borohydride reduction of the bromo-ketone, in methanol and in *tert.*-butanol, was (after acetylation) the starting ketone (I). It is suggested that as even unsubstituted 11-ketones are only reduced slowly by an excess of sodium borohydride (cf. Heymann and Fieser, *ibid.*, 1951, **73**, 5252; Oliveto and Hershberg, *ibid.*, 1953, **75**, 488) the nucleophilic attack by the reagent occurs alternatively at bromine to give the enolate ion of the 11-ketone.

Reduction with lithium aluminium hydride gave somewhat different results and provided proof that bromine is attached at $C_{(9)}$ in the bromo-ketone. With sufficient reagent to reduce the 11-oxo- and the 3β-acetoxy-group the 9β : 11β-epoxide (III; after reacetylation) was isolated in 50% yield; this appears to arise by hydride attack on the carbonyl group at $C_{(11)}$ followed by displacement of bromide ion. The epoxide was accompanied by some 30% of 3β-acetoxyergostan-11β-ol (IV): this could have been formed by further reduction of the 9β : 11β-epoxide, but it is more likely that debromination (as observed with sodium borohydride) is occurring as a competing reaction, the 11-ketone being relatively rapidly reduced to the 11β-ol. Authentic 9β : 11β-epoxide was prepared by conversion of the appropriate Δ^9-compound (*J.*, 1954, 731) into the 9α-bromo-11β-hydroxy-steroid followed by dehydrobromination with potassium *tert.*-butoxide. As Fried and Sabo (*J. Amer. Chem. Soc.*, 1953, **75**, 2273) have reported, the yield of bromohydrin is greatly improved by using perchloric instead of sulphuric acid.



Further indication of the $C_{(9)}$-location of the bromine atom was provided by dehydrobromination by collidine or by silver nitrate in pyridine (pyridine alone was ineffective), the known, conjugated Δ^8-11-ketone (*J.*, 1953, 2921) then being formed. An α-configuration is assigned for the 9-bromine substituent from its method of formation; the lack of appreciable shift of the carbonyl stretching frequency is in agreement with this.

Tertiary bromo-ketones can usually be isomerized to more stable secondary bromo-compounds (cf. Heilbron, Jackson, Jones, and Spring, *J.*, 1937, 801; 1938, 102; Inhoffen and Zühlsdorff, *Ber.*, 1943, **76**, 233). Preliminary experiments have shown that hydrogen bromide will convert the bromo-ketone (II) into an isomer which appears to be the 12α-bromo-compound; a more detailed study of this reaction is being made. The formation of the 9-bromo-compound from the ergostanone (I) is in accord with the known direction of enolization of 11-ketones of the 5α-series, Δ^9-11-acetates being formed on

acetylation. Δ^9-11-Acetates are also formed from 11-ketones in the 5β-series, and the isolation of a 12-bromo-ketone by Turner *et al.* (*loc. cit.*) may be due to the greater steric crowding associated with bromination at $C_{(9)}$ in the 5β-series, which may result in bromination at $C_{(12)}$ or in ready rearrangement of bromine from $C_{(9)}$ to $C_{(12)}$.

Experimental

M. p.s were recorded on a Kofler block and are corrected. Rotations were determined in chloroform solutions.

3β-Acetoxy-9α-bromoergostan-11-one (II).—A solution of 3β-acetoxyergostan-11-one (2·8 g.) in acetic acid (18 c.c.) was treated successively with hydrobromic acid (50% in acetic acid; 5 drops) and bromine (0·32 c.c.; 1·1 mol.) in acetic acid (3·2 c.c.), whereafter the solution was heated at 40° until the bromine colour was discharged. These operations were performed with nitrogen bubbling through the solution, and the reaction vessel shielded from light. Much of the bromo-compound crystallized when the mixture cooled, but the total product was isolated *via* ether. Crystallization from methanol–acetone gave fairly pure product (3·05 g.); further crystallization afforded the pure *bromo-ketone* as plates, m. p. 161—163°, $[\alpha]_D$ +128° (Found: C, 66·95; H, 9·4; Br, 14·6. $C_{30}H_{49}O_3Br$ requires C, 67·0; H, 9·25; Br, 14·9%). Infrared spectrum (in CS_2) = peaks at 1735, 1245 (acetate), and 1710 cm.$^{-1}$ (11-ketone).

3β-Acetoxy-9β : 11β-epoxyergostane (III).—(*a*) An ether solution (20 c.c.) of the bromo-ketone (376 mg.) and lithium aluminium hydride (22 mg.; 0·83 mol.) was heated under reflux for 1 hr. The product was isolated with ether, acetylated, and chromatographed on deactivated alumina (30 g.). Elution with light petroleum–benzene (10 : 1) gave *3β-acetoxy-9β : 11β-epoxyergostane* (150 mg.), m. p. 114—115° (from acetone–methanol), $[\alpha]_D$ +23° (Found: C, 78·35; H, 11·05. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%). Infrared spectrum: no hydroxyl band. Elution with light petroleum–benzene (1 : 1) gave 3β-acetoxyergostan-11β-ol (80 mg.), m. p. and mixed m. p. 133—134° (from methanol), $[\alpha]_D$ +28°.

(*b*) A solution of 3β-acetoxy-9α-bromoergostan-11β-ol (225 mg.) in *tert.*-butanol (20 c.c.) was treated with M-potassium *tert.*-butoxide (2 c.c.) solution in *tert.*-butanol. The solution was kept at 50° for 15 min.; the steroid was isolated with ether, acetylated, and crystallized from methanol–acetone to yield the 9β : 11β-epoxide (120 mg.), m. p. and mixed m. p. 113—115°.

3β-Acetoxy-9α-bromoergostan-11β-ol.—A solution of 3β-acetoxyergost-9-ene (1·13 g.) in ether (30 c.c.) and acetone (100 c.c.) containing water (9 c.c.) and N-perchloric acid (1 c.c.) was added to a solution of *N*-bromosuccinimide (700 mg.) in acetone (50 c.c.). The mixture was kept at 0° for 4 hr., then sodium sulphite solution was added followed by sodium carbonate solution until the solution was alkaline. Addition of water (500 c.c.) precipitated the product, which when crystallized from aqueous acetone afforded the *bromohydrin* (1 g.; m. p. 159—162°), $[\alpha]_D$ +28° (Found: C, 67·2; H, 9·7. $C_{30}H_{51}O_3Br$ requires C, 66·8; H, 9·45%). Infrared spectrum (in CCl_4): peaks at 3620 (hydroxyl), 1730, and 1245 cm.$^{-1}$ (acetate).

Sodium Borohydride Reduction of the Bromo-ketone (II).—The hydride (450 mg.) was added to a solution of the bromo-ketone (1 g.) in methanol (150 c.c.), the mixture then being heated under reflux for 12 hr. The steroid was isolated with ether, acetylated, and chromatographed on deactivated alumina (50 g.). Elution with light petroleum–benzene (10 : 1) gave 3β-acetoxyergostan-11-one (400 mg.), m. p. and mixed m. p. 138—139°, $[\alpha]_D$ +34°. Elution with light petroleum–benzene (1 : 1) yielded 3β-acetoxyergostan-11β-ol (60 mg.), m. p. and mixed m. p. 132—133°.

An identical experiment with *tert.*-butanol instead of methanol afforded the same products, the ketone : 11β-alcohol ratio being slightly lower.

3β-Acetoxyergost-8-en-11-one from the Bromo-ketone (II).—A solution of the bromo-ketone (500 mg.) in collidine (25 c.c.) was heated under reflux for 2 hr. in nitrogen. Isolation with ether and crystallization from methanol gave the conjugated ketone (300 mg.) as needles, m. p. 135—137°, $[\alpha]_D$ +116°. Light absorption (in EtOH): $\lambda_{max.}$ 2540 Å; $\varepsilon_{max.}$ 10,000. When a solution of the bromo-compound (750 mg.) in pyridine (20 c.c.) containing silver nitrate (2·5 g.) was heated under reflux for 5 hr., a good yield of the conjugated ketone was also obtained.

The authors thank Glaxo Laboratories Ltd., for gifts of materials, and the Department of Scientific and Industrial Research for Maintenance Grants to (to A. A. W. and T. I. W.). Microanalyses were performed by Messrs. E. S. Morton and H. Swift, and the infrared spectra were determined under the direction of Dr. G. D. Meakins.

The University, Manchester, 13. [*Received, February 17th*, 1955.]

The Hydrothermal Chemistry of Silicates. Part VI. A Lamellar Habit in Synthetic Felspar.*

By J. A. Gard, R. M. Barrer, and J. Baynham.

[Reprint Order No. 6143.]

Very thin lamellar crystals of synthetic potash felspar have been found associated in some preparations with major yields of synthetic leucite and in others with major yields of synthetic felspar of normal prismatic habit. 010 surfaces of the lamellæ were highly developed, while $1k0$, $0kl$, and $1k\bar{l}$ were also common. The 010 surfaces of a small number of the lamellar crystals had straight shallow steps parallel to the *c*-axis and no more than a very small number of unit cells high. These appear to be growth steps.

Studies from these laboratories have been concerned with syntheses and properties of crystalline aluminosilicates of Li (Barrer and White, *J.*, 1951, 1167), Na (*idem*, *ibid.*, 1952, 1561; Barrer and Bultitude, in preparation), Rb (Barrer and McCallum, *J.*, 1953, 1466, 4029), Cs (*ibid.*, p. 1466), and Tl (*ibid.*, p. 4029; Taylor, *J.*, 1949, 1253). In a corresponding study (Barrer and Baynham, unpublished work) of the crystallisation field of potassium aluminosilicates, lamellar crystals were observed with some interesting features now to be described.

The techniques used by us in hydrothermal crystallisation have been discussed in earlier papers of this series, reactions being carried out in steel autoclaves. Reaction products were examined optically, by *X*-ray powder photography, and, particularly in this paper, with a Metropolitan Vickers M-V EM3 electron microscope in which electron-diffraction patterns of small areas of the specimens can be recorded.

By means of the electron microscope, lamellar crystals, such as those shown in Figs. 1 and 2, were discovered in minor yields. They were associated in certain preparations with major yields of synthetic leucite; in others, with major yields of synthetic potash felspar of normal prismatic habit. The leucite and associated lamellar crystals were grown from 0·5 g. of an aluminosilicate gel of molar composition $K_2O : Al_2O_3 : SiO_2 = 1 : 1 : 3$ with 0·3 g. of potassium hydroxide and 10 ml. of water. The mixture was heated in a 15-ml. steel autoclave at 300° for 3 days. The prismatic potash felspar crystals and associated lamellar crystals were grown from more siliceous gels of several compositions. For example, 0·5 g. of an aluminosilicate gel of composition $K_2O : Al_2O_3 : SiO_2 = 1 : 1 : 5$ was heated with 51% molar excess of potassium hydroxide in water for 4 days at 250°.

Identification of Lamellar Crystals.—Unit-cell determinations of the lamellar crystals were made by electron diffraction. The diffraction pattern (*e.g.*, Fig. 3) is a projection of the reciprocal lattice of a number of atom planes perpendicular to the electron beam, divided into approximately circular Laue zones, due to scattering from the row of lattice points most nearly parallel to the electron beam. Unit-cell dimensions can be determined from the distances between rows of spots and the radii of the circular Laue zones. The Table summarises unit-cell dimensions of several potash felspars and of two

Unit cells of lamellar crystals and of potash felspars.

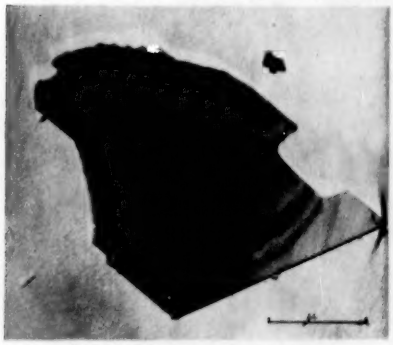
Unit-cell dimension	Lamellar crystals (1)	Lamellar crystals (2)	Orthoclase	Sanidine	Microcline
a	8·49 (±0·15)	8·43 (±0·09)	8·45	8·40	8·44
c	7·08 (±0·07)	7·05 (±0·11)	7·15	7·10	7·21
β	116—117°	115—117°	116° 3′	115° 35′	155° 50′
b	12·8 (±0·33)	12·7 (±0·22)	12·90	12·90	13·00

of the lamellar crystals, one associated with leucite and one with prismatic potash felspar. The lamellar crystals clearly have a unit cell very close to those of the potash felspars. The "*b*"-dimension, being determined from the radii of the Laue zones, is the least accurate.

Further to confirm the identity of the lamellæ with felspar, natural orthoclase was

* Part V, *J.*, 1953, 4035.

FIG. 1. *Laminar crystal of potash felspar.*

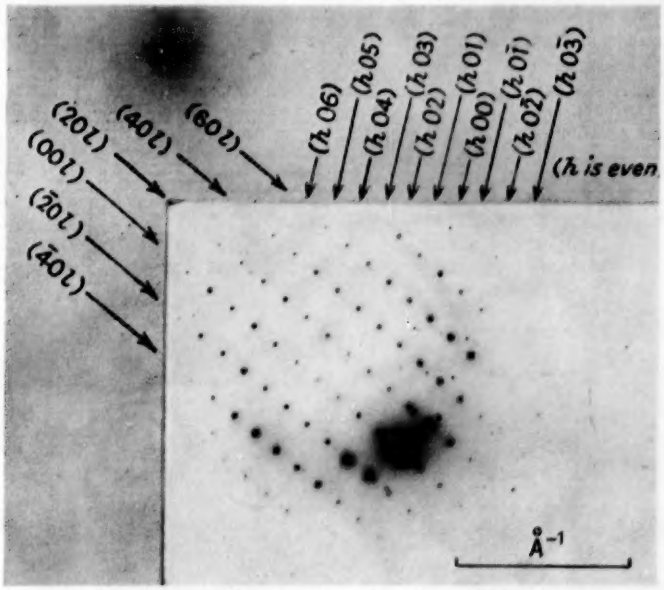


The continuous step along one edge resembles those of layer lattice minerals.

FIG. 2. *Crystals of potash felspar.*

The larger crystal has six steps parallel to its long edge. The smaller is *ca.* 70 Å thick (5—6 unit cells).

FIG. 3. *Electron-diffraction pattern of lamellar crystal of potash felspar,* 2000 Å *thick.*

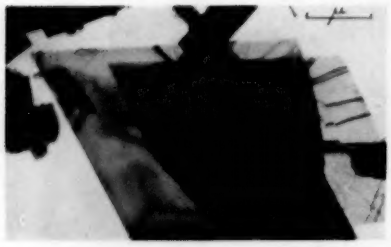


The 010 planes are perpendicular to, and the *b*-axis parallel to, the electron beam.

[*To face p.* 2480.

FIG. 4. *Pairs of similarly oriented and shaped lamellar potash felspar crystals.*

a



b

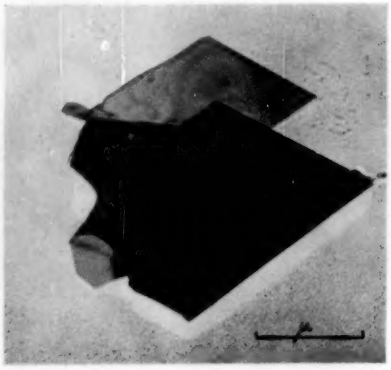
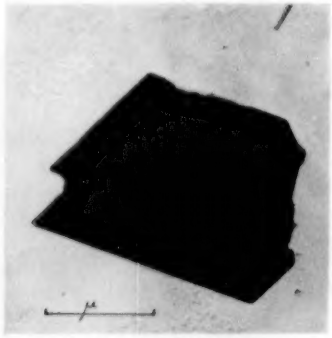


FIG. 5. *Crystals of potash felspar with regular depressions on the surfaces.*

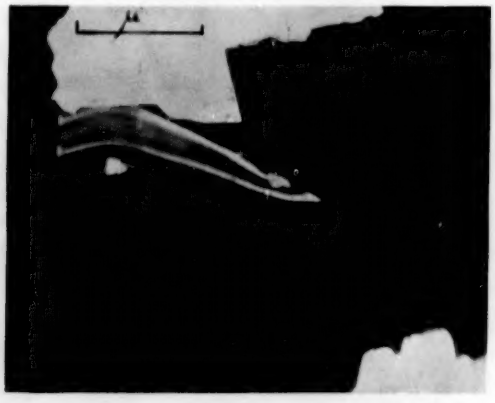
a

b



The crystal (*a*) has V-shaped grooves, and parallel growth steps which are not continuous across the grooves. This suggests that growth has been initially around an obstruction which has later been displaced. The crystal (*b*) has a triangular notch and a flat depression at the upper edge.

FIG. 6. *Crystal of potash felspar, showing a shallow platform, with one growth step towards the edge on the left, and several parallel steps towards the point on the right.*



finely ground and individual crystal pieces were examined by electron diffraction. Only a few patterns similar to those given by the lamellæ were observed, since the number of pieces with orientation in the electron beam the same as the lamellæ (*i.e.*, *b*-axis parallel to the beam) was very limited. However, this experiment supports the identification of the lamellæ as potash felspar. Mineralogical works record such a habit, although the extreme thinness of the present crystal flakes is quite unusual.

Topography and Growth Layers.—The lamellæ were small compared with the normal prismatic felspar crystals among which they were found. The finest specimen was only about 70 Å in thickness. The 010 surfaces (the faces of the lamellæ) were normally perfectly plane, and of variable shape. Most crystals showed two or more other faces, one of which always corresponded to 1*k*0, while 0*kl* and 1*kl* were also common. Pairs of similarly shaped crystals are seen in Fig. 4. Several crystals (*e.g.*, Fig. 5) showed V-shaped grooves in the 010 surface. Probably the crystals grew round prismatic crystals which became dislodged later.

Among the lamellar crystals associated with leucite was a small proportion in which the 010 surfaces were traversed from edge to edge by a number of parallel straight marks, which were shown by shadow casting to be shallow steps (Figs. 2, 5*a*, 6). Fig. 6 shows a crystal with a shallow platform with steps leading from it to both extremities of the flake. The parallel steps were invariably in the direction of the *c*-axis. No accurate estimate of the height of each step was possible but this height was probably less than 25 Å. The steps almost certainly represent the terminations of successive growth layers. In Fig. 5*a*, where the 010 surface was broken by the regular depressions already described, the steps did not usually correspond on opposite sides of a depression, indicating different rates of advance of the growth layers on the two sides. These growth layers are not compatible with crystal growth from screw dislocations (*e.g.*, Frank, *Discuss. Faraday Soc.*, 1949, **5**, 48), but represent an alternative mode of growth likely to be important at higher degrees of supersaturation.

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The Reaction of Indolylmagnesium Iodide with Enol-lactones of γ-Keto-acids.

By A. R. KATRITZKY and SIR ROBERT ROBINSON.

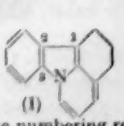
[Reprint Order No. 6184.]

Indolylmagnesium iodide has been shown to react with 4 : 5-dihydro-5-oxo-2-phenylfuran, α-angelicalactone and γ-oxopimelic anhydride to give 1-acylated indoles. 1-Lævuloylindole has been cyclised to 3-methyl-1 : 2-(2′ : 7′)-benzylenepyrid-6-one, the action of alcoholic alkali on which supports an explanation previously advanced for the yellow colour and green fluorescence frequently encountered in alcoholic alkaline solution of certain strychnine derivatives.

IT has been shown that 2 : 3-benzopyrrocolines are alkylated in the 1-position (Robinson and Saxton, *J.*, 1952, 976); thus the derivative (I) should yield the pyridinium salt (II) which is of interest in simulating a portion of the strychnine molecule.

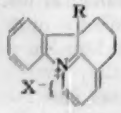
A possible route to the tetracyclic skeleton (I) would be the condensation of indole with the readily available γ-oxopimelic acid in three positions as shown in (III). However this could not be done directly, for indole shows maximum activity towards cationoid reagents at the 3 (or sometimes 1-position) whereas the cationoid activity of the keto-group in pimelic acid, which it is desired to condense with position 2 of the indole, is greater than that of the carboxyl groups. It is, however, possible to reverse this order of reactivity by the use of enol-lactones (or a dilactone) instead of the keto-acids.

Although in general γ- and δ-keto-acids and their esters are attacked by Grignard reagents at the carbon atom of the keto-group, yet in the enol-lactones derived from them the carbon atom of the carboxyl group would be expected to become the centre for attack by anionoid reagents. This type of reaction has recently been used with enol-δ-lactones

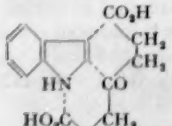


(I)

(The numbering refers to pyrrocoline itself.)

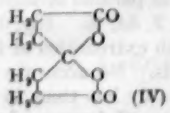


(II)



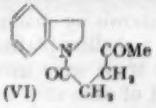
(III)

to introduce $C_{(4)}$ of the steroid nucleus (Fujimoto, *J. Amer. Chem. Soc.*, 1951, **73**, 1856; Woodward, Sondheimer, Taub, Heuster, and McLamore, *ibid.*, 1952, **74**, 4223; Wieland, Weberwasser, Anner, and Miescher, *Helv. Chim. Acta*, 1953, **36**, 1231), but no example of the reaction of an enol-γ-lactone with a Grignard reagent appears to have been recorded.



(IV)

(V)



(VI)

γ-Oxopimelic acid does not form an enol-lactone, but the above considerations apply also to the dilactone (IV). As a preliminary to work with this dilactone, it was decided to investigate the reaction of indolylmagnesium iodide with the simpler α-angelicalactone (V; R = Me) and 4 : 5-dihydro-5-oxo-2-phenylfuran (V; R = Ph), *i.e.*, the enol-lactones of lævulic acid and β-benzoylpropionic acid.

The reactions of indolylmagnesium halides have been extensively investigated and, in accordance with the hybrid nature of the indole anion, although in the majority of cases the 3-substituted indole is produced, it is sometimes accompanied by the 1-substituted or the 1 : 3-disubstituted indole (*e.g.*, Oddo, *Gazzetta*, 1911, **41**, 221, 234). The dependence of the orientation on solvent and temperature has been reported in special cases: Alexandri (*Atti R. Accad. Lincei*, 1915, **24**, II, 194) obtained 1-formylindole with only small amounts of 3-formylindole from ethyl formate in ether; Majima and Kotake (*Ber.*, 1922, **55**, 3859) used anisole as a solvent and isolated mainly 3-formylindole. The latter authors found (*ibid.*, p.3865) that the yield of 3-substituted products was in general higher with this solvent except in reactions with acid chlorides. Potokhin (*J. Russ. Phys. Chem. Soc.*, 1927, **59**, 761; *Chem. Abs.*, 1928, **22**, 3409) used benzene as solvent and found that, with ethyl formate at 0° the 1-derivative was formed, but at 85° 3-formylindole.

When 4 : 5-dihydro-5-oxo-2-phenylfuran (V; R = Ph) was allowed to react with preformed indolylmagnesium iodide in ether, only one product was isolated, which analysed correctly for a mono-(β-benzoylpropionyl)indole and could have been either the 1- or the 3-substituted product. A distinction could easily be made, for it is known that 1-acylindoles are readily hydrolysed by warm dilute alkali whereas 3-acylindoles are unaffected (*e.g.*, Saxton, *J.*, 1952, 3592); under these conditions the compound underwent cleavage to β-benzoylpropionic acid and indole and was thus shown to be 1-β-benzoylpropionylindole. This conclusion was supported by the infrared spectrum which showed no band at 2·90—2·94 μ; this band is given by all indoles which are not 1-substituted (Brown, Henbest, and Jones, *J.*, 1952, 3174). 1-β-Benzoylpropionylindole was characterised as the 2 : 4-dinitrophenylhydrazone and semicarbazone. The reaction between indolylmagnesium iodide and 4 : 5-dihydro-5-oxo-2-phenylfuran was carried out eight times under different conditions, ether and anisole being used as solvent and temperature and duration of the reaction varied. Under those conditions that appear to favour 3-substitution (see above), small amounts of by-products were formed, but 1-β-benzoylpropionylindole was the only pure substance isolated.

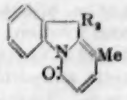
When α-angelicalactone (V; R = Me) was caused to react with indolylmagnesium iodide in ether (or in anisole) the product was a viscous red oil which did not crystallise

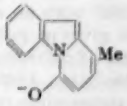
even on being seeded with material from an earlier run. However, a homogeneous lævuloylindole semicarbazone could be prepared which, on being refluxed with pyruvic acid in dilute acetic acid (cf. Hershberg, *J. Org. Chem.*, 1948, **13**, 542), was reconverted into the parent compound. Ready alkaline hydrolysis to lævulic acid and indole showed this compound to be 1-lævuloylindole (VI), and this was confirmed by the absence of an N–H band in the infrared spectrum. 1-Lævuloylindole was further characterised as the 2 : 4-dinitrophenylhydrazone and oxime.

The reaction of the dilactone (IV) with indolylmagnesium iodide gave very similar results to those recorded above for α-angelicalactone. An oil was formed affording a semicarbazone which was decomposed with pyruvic acid, and the product was proved to be 1-(6-carboxy-4-oxohexanoyl)indole by reason of its sensivity to alkali and its infrared spectrum. The methyl ester was prepared with the aid of diazomethane; it afforded a 2 : 4-dinitrophenylhydrazone.

Many attempts were made to cyclise the foregoing 1-oxoacylindoles using (i) phosphoric anhydride in boiling toluene, (ii) phosphoryl chloride alone or with chloroform, cold or at the b. p., (iii) polyphosphoric acid at 150°, (iv) boron trifluoride in chloroform, (v) sulphuric acid, (vi) hydrogen chloride in ethyl acetate, and (vii) refluxing acetic anhydride, with or without zinc chloride. After many trials a crystalline perchlorate was isolated from the product of 1-lævuloylindole and sulphuric acid, from which the cyclised base was obtained with ammonia. This was shown to be 3-methyl-1 : 2(2′ : 7′)-benzylenepyrid-6-one (VII; R = H), and not a double bond isomer of this, by comparison of the infrared spectrum with that of 3 : 7′ : 7′-trimethyl-1′ : 7′(1 : 2)-benzylenepyrid-6-one (VII; R = R = Me) (Robinson and Saxton, *loc. cit.*). Unfortunately all efforts to cyclise the other 1-oxoacylindoles failed and this led to the abandonment of that line of research.

In work involving the treatment of strychnine derivatives with alcoholic alkali, it has been frequently observed that a brownish-yellow solution exhibiting characteristic green fluorescence is produced. This is formed, for example, from strychnine in warm alcoholic potassium hydroxide in presence of air. Woodward, Brehm, and Nelson recognised strychnone as an aromatic-type indole derivative (*J. Amer. Chem. Soc.*, 1947, **69**, 2250), and Bailey and Robinson in expressing similar views about bruzone (*Nature*, 1948, **161**, 433) took the opportunity to attribute the above-mentioned colour and fluorescence to the formation of a hydroxybenzopyrrocoline system.

(VII) 



(VIII)

The substance (VII; R = H) (but not R = Me) develops a brownish-yellow solution with green fluorescence in warm alcoholic potassium hydroxide and this is probably due to the anion (VIII). The exhibition of this property strongly supports the suggestion of Bailey and Robinson.

Experimental

1-β-*Benzoylpropionylindole.*—A solution of indole (3·51 g.) in ether (15 c.c.) was gradually added, at 0°, with stirring, to one of methylmagnesium iodide (magnesium 0·87 g.; methyl iodide, 4·8 g.; ether, 50 c.c.). After the solution had been refluxed for 15 min. and cooled again to 0°, 4 : 5-dihydro-5-oxo-2-phenylfuran (4·5 g.) (Kugel, *Annalen*, 1898, **299**, 54) in ether (70 c.c.) was added. The mixture was refluxed for 15 min. and the complex decomposed at 0° by water (50 c.c.) and 2N-acetic acid (46 c.c.). A part of the *product* gradually crystallised and a further quantity was obtained from the ethereal layer (total yield, 2·8 g., 37%). Two recrystallisations from ethanol gave colourless needles, m. p. 147—149° (Found: C, 78·2; H, 5·6; N, 5·1. $C_{18}H_{15}O_2N$ requires C, 78·0; H, 5·4; N, 5·1%). The Ehrlich reaction was a cherry-red coloration. The 2 : 4-*dinitrophenylhydrazone* was prepared in alcoholic solution containing hydrochloric acid, and after chromatographic purification (alumina–benzene) crystallised from acetic acid as yellow needles, m. p. 231—232° (Found: C, 62·7; H, 4·2. $C_{24}H_{19}O_5N_5$ requires C, 63·0; H, 4·2%). The *semicarbazone*, prepared in pyridine, crystallised

from ethanol in prisms, m. p. 178—180° (Found : C, 68·4; H, 5·6. $C_{19}H_{16}O_3N_4$ requires C, 68·2; H, 5·4%).

1-β-Benzoylpropionylindole (0·2 g.) was heated with aqueous 5% sodium hydroxide (6 c.c.) and ethanol (1·5 c.c.) for 4 hr. at 60°. The whole was extracted with benzene, and indole picrate, m. p. and mixed m. p. 180—183° (decomp.), was isolated from the hydrocarbon layer with picric acid. The semicarbazone of β-benzoylpropionic acid was obtained from the aqueous layer. It had m. p. 207—208° (decomp.), undepressed on admixture with an authentic specimen [Attwood, Stevens, and Thorpe, *J.*, 1923, **123**, 1762, give m. p. 206° (decomp.)].

Indole picrate separated from benzene as red needles, m. p. 181—185° (decomp.) (Found : C, 48·7; H, 3·2. Calc. for $C_{14}H_{10}O_7N_4$: C, 48·6; H, 2·9%). Baeyer and Caro (*Ber.*, 1877, **10**, 1263; 1879, **12**, 1314) quote an analysis for this compound, but no m. p. seems to have been recorded.

1-*Lævuloylindole* (VI).—A solution of α-angelicalactone (19·6 g.) (prepared by the method of Thiele, Tischbein, and Lossow, *Annalen*, 1902, **319**, 184) in ether (50 c.c.) was added, gradually, with stirring, at 0°, to one of indolylmagnesium iodide, prepared from indole (23·4 g.) as above, and the solution was stirred at room temperature for 30 min. and refluxed for 15 min. Water (260 c.c.) and acetic acid (36 c.c.) were added at 0°. The ethereal layer was separated and the ether removed. The residual red oil was warmed to 70—80° with pyridine (150 c.c.), and semicarbazide hydrochloride (18 g.) in water (18 c.c.) was added; *1-lævuloylindole semicarbazone* (22·3 g., 41%) began to separate in prisms almost immediately. After a few hours it was collected and washed eight times with cold ethanol; the m. p. was 210—212°, raised by two crystallisations from a large volume of ethanol to 216° (Found : C, 62·3; H, 6·0. $C_{14}H_{16}O_2N_4$ requires C, 61·8; H, 5·9%). A mixture of this semicarbazone (22·3 g.), acetic acid (300 c.c.), and pyruvic acid (13 g.) was refluxed for 15 min. and, while it was still boiling, water (300 c.c.) was added gradually during 10 min., followed by more water (500 c.c.) added all at once. On cooling slowly, *1-lævuloylindole* (14 g., 79%) separated in needles; after recrystallisation from ethanol–water (1 : 1) these had m. p. 78—79° (Found : C, 72·4; H, 6·1. $C_{13}H_{13}O_2N$ requires C, 72·6; H, 6·0%). The substance gave a deep purple-red Ehrlich reaction. The 2 : 4-*dinitrophenylhydrazone*, prepared in acid ethanol and purified by chromatography (alumina–benzene) separated from toluene in yellow prisms, m. p. 214—215° (Found : C, 57·3; H, 4·3. $C_{19}H_{17}O_6N_5$ requires C, 57·7; H, 4·3%). The *oxime*, prepared in pyridine, separated from ethanol–water (1 : 1) as plates, m. p. 138° (Found : C, 67·4; H, 6·2. $C_{13}H_{14}O_2N_2$ requires C, 67·8; H, 6·1%). Treatment of lævuloylindole overnight with aqueous 2N-sodium hydroxide, followed by extraction with benzene, led to the isolation of indole (picrate, m. p. and mixed m. p. 180—183°) from the benzene layer, and lævulic acid (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 203—205° with an authentic specimen of m. p. 204—206°; Strain, *J. Amer. Chem. Soc.*, 1935, **57**, 758, gives m. p. 206°) from the aqueous solution.

γ-Oxopimelic Dilactone (2 : 2′-spiro*Tetrahydropyran-5-one*) (IV).—γ-Oxopimelic acid (40 g.) (U.S.P. 2,436,532; *Chem. Abs.*, 1948, **42**, 5048) and acetic anhydride (60 c.c.) were refluxed for 2½ hr., and volatile compounds removed at 100°/13 mm. Addition of a little chloroform–ethanol (1 : 10) to the residue gave the anhydride (32·4 g., 90%) which after crystallisation from the same solvent had m. p. 60—61°, unchanged by further recrystallisation (Found : C, 54·0; H, 4·9. Calc. for $C_7H_8O_4$: C, 53·8; H, 5·1%). Volhard (*Annalen*, 1889, **253**, 221) gives m. p. 75°, and later (*ibid.*, 1892, **267**, 105), m. p. 69°; Michael (*J. prakt. Chem.*, 1891, **44**, 118) gives m. p. 64—65°.

1-(6-*Carboxy*-4-*oxohexanoyl*)*indole*.—γ-Oxopimelic dilactone (30·8 g.) in anisole (30 c.c.) was brought into reaction with indolylmagnesium iodide (from indole, 23·2 g.) in a similar manner to that described above for the preparation of 1-lævulylindole. 1-(6-*Carboxy*-4-*oxohexanoyl*)-*indole semicarbazone* (17 g., 26%) separated from pentyl alcohol in prisms, m. p. 189—190° (Found : C, 58·2; H, 5·9. $C_{16}H_{19}O_4N_4$ requires C, 58·2; H, 5·5%). This derivative (17 g.) was decomposed with pyruvic acid essentially as before, to give the parent *indole* (10·8 g., 77%), which crystallised from aqueous ethanol (1 : 1) in needles, m. p. 126—126·5° (Found : C, 66·1; H, 5·4. $C_{16}H_{15}O_4N$ requires C, 65·9; H, 5·5%). The Ehrlich test gave a cherry-red colour. The *methyl ester*, prepared in 95% yield by means of ethereal diazomethane, crystallised from methanol in needles, m. p. 73—73·5° (Found : C, 66·5; H, 5·9. $C_{16}H_{17}O_4N$ requires C, 66·9; H, 5·9%). The methyl ester gave a 2 : 4-*dinitrophenylhydrazone* which, after chromatographic purification (alumina–benzene–ether), separated from ethanol in yellow needles, m. p. 144—146° (Found : C, 56·5; H, 4·5. $C_{22}H_{21}O_7N_5$ requires C, 56·5; H, 4·5%). 1-(6-Carboxy-4-oxohexanoyl)indole was hydrolysed as described above for 1-lævuloylindole, to give indole picrate, m. p. and mixed m. p. 181—185°, and γ-oxopimelic acid semicarbazone, m. p. and mixed m. p.

196° (decomp.) (Asahina and Fujita, *Acta Phytochim.*, 1922, **1**, 33; Beilstein's "Handbuch," Suppl. II, Vols. III/IV, p. 487, give m. p. 204°).

3-Methyl-1 : 2(2' : 7')benzylenepyrid-6-one (VII; R = H).—Concentrated sulphuric acid (15 c.c.) was poured on 1-lævuloylindole (15 g.). The mixture became hot and the solid dissolved to a red solution which was kept an hour and then added to a mixture of acetic acid (25 c.c.) and perchloric acid (32 c.c. of 60%). The *perchlorate* (7·3 g., 36%) which separated recrystallised from acetic acid as needles, m. p. 275° (explosive decomp.) (Found: C, 52·9; H, 3·9. $C_{13}H_{12}O_6NCl$ requires C, 52·5; H, 4·0%). The perchlorate (12 g.) was shaken with chloroform (60 c.c.), water (30 c.c.), and aqueous ammonia (*d* 0·88; 40 c.c.) for a few minutes, all the solid dissolving. Solvent was removed from the dried chloroform layer, and the product crystallised from acetic acid. The *pyridone* separated in colourless needles, m. p. 154—155·5° (Found: C, 79·2; H, 5·6; N, 7·1. $C_{13}H_{11}ON$ requires C, 79·2; H, 5·6; N, 7·1%). The substance does not give a colour with Ehrlich's reagent. When the pyridone was boiled with ethanol and solid potassium hydroxide added, a brown-yellow solution was formed and this exhibited an intense green fluorescence; it soon faded when shaken in air.

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The Dyson Perrins Laboratory, Oxford University. [*Received, March 2nd*, 1955.]

The Thermochemistry of Organic Phosphorus Compounds. Part I. Heats of Hydrolysis and Oxidation.

By E. Neale and L. T. D. Williams.

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In order to obtain data on the heats of formation of organic phosphorus compounds for which the usual methods of combustion calorimetry proved unsatisfactory, a number of typical reactions have been studied in a simple Dewar vessel calorimeter. Although the information thus obtained does not necessarily permit the direct computation of heats of formation, it does enable approximate values to be assigned for "average bond-energy terms" which can be used to estimate heats of formation or reaction. The present paper deals with hydrolytic and oxidative reactions.

This investigation was undertaken to obtain preliminary values for the heats of formation of some simple organic compounds of phosphorus. Comparatively little work has been done on the thermochemistry of phosphorus and, with the exception of methylphosphonic acid reported by Thompson (*J.*, 1952, 3292) after the commencement of this work, no organophosphorus compounds have been studied hitherto.

One reason for this lack of data is the difficulty, experienced by both Thompson and ourselves, of securing complete combustion and of determining the precise stoicheiometry of the bomb reaction with phosphorus compounds. We were therefore compelled to resort for the most part to reaction calorimetry, for which purpose we were able to find a number of convenient reactions, but the data obtained were of course dependent on the heats of formation accepted for the parent substances, phosphorous acid, orthophosphoric acid, and phosphorus trichloride and oxychloride. The values given in "Selected Values of Chemical Thermodynamic Properties" (National Bureau of Standards, Circular 500) are based on determinations carried out some eighty years ago and only in the case of orthophosphoric acid are more recent data available, confirming the earlier work. In a note (*J.*, 1952, 4535) we gave revised values for the two chlorides, and these results were supported reasonably well by the independent work of Charnley and Skinner (*J.*, 1953, 450) carried out at about the same time.

In this work, the N.B.S. Circular 500 values were used for heats of formation of phosphorous and phosphoric acids but in view of the uncertainty regarding the former, the heat of formation of the trichloride was redetermined by simultaneous hydrolysis and

oxidation, thus enabling $\Delta H_f^\circ(H_3PO_4)$ rather than $\Delta H_f^\circ(H_3PO_3)$ to be used in the computation. This work has also been published by us (*J.*, 1954, 2156).

This paper reports the heats of hydrolysis of several phosphorus halides and other compounds, and the heats of oxidation of some compounds of tervalent phosphorus. The data obtained are used to derive heats of formation, where possible, and values for the relevant " average bond energies " (cf. Cottrell and Sutton, *Quart. Reviews*, 1948, **2**, 260). In a later paper it is intended to report similar data on heats of esterification and anilide formation, and heats of combustion of some anilides formed from phosphorus halides.

Experimental

Preparation of Compounds.—(i) Methyl and ethylphosphonic dichlorides: by hydrolysis of the complex of the appropriate alkyl chloride with phosphorus trichloride and aluminium chloride (Kinnear and Perren, *J.*, 1952, 3437). (ii) Tri*iso*propyl phosphite: by Ford-Moore and Perry's method (*Org. Synth.*, **31**, 111). (iii) Diethyl hydrogen phosphite: by esterification of the trichloride in the absence of base (McCombie, Saunders, and Stacey, *J.*, 1945, 380). (iv) Ethyldichlorophosphine: by treatment of tetraethyl-lead with phosphorus trichloride (Kharasch, Jensen, and Weinhouse, *J. Org. Chem.*, 1949, **14**, 429). (v) Tetraethyl pyrophosphate: treatment of the silver salt of diethyl hydrogen phosphate with diethyl chlorophosphonate (details of this preparation will be published later). (vi) Diethyl phosphorofluoridate: by Saunders and Stacey's method (*J.*, 1948, 695).

The method used for the preparation of *iso*propyl methylphosphonochloridate will be published later.

All materials were purified by repeated distillation under reduced pressure, the tervalent phosphorus compounds being distilled under nitrogen. Purity was checked by hydrolysis and acidimetry for the halides and the pyrophosphate, and by reaction with iodine buffered with bicarbonate for the phosphite esters. Refractive indices agreed well with published data where available (see below) and infrared spectra gave no evidence of impurity except for tri*iso*propyl phosphite where a trace of phosphate was indicated. In the latter case purity was assessed at 98·5%; all other compounds came within the range 99·0—99·8% purity.

	B. p. (M. p.)	n_D^{25}
Methylphosphonic dichloride	86°/44 mm. (33°)	—
Ethylphosphonic dichloride	65°/5 mm.	1·4630
Diethyl phosphorofluoridate	63°/12 mm.	1·3724
Diethyl hydrogen phosphite	77°/17 mm.	1·4064
Tri*iso*propyl phosphite	43°/1 mm.	1·4080
*iso*Propyl methylphosphonochloridate	47°/3 mm.	1·4280
Ethyldichlorophosphine	112°/760 mm.	—
Tetraethyl pyrophosphate	110°/0·05 mm.	1·4176

Procedure.—The calorimeter was of the Dewar-vessel type described previously (*loc. cit.*); it was calibrated electrically. The samples were contained in glass ampoules which were broken under the surface of the liquid; they were filled in a glove-box through which dry air was circulated (dry nitrogen was used when handling tervalent phosphorus compounds). All measurements were carried out between 22° and 23°.

Hydrolytic reactions were carried out in distilled water where possible, but in a few cases, noted below, aqueous sodium hydroxide was necessary. For the oxidation of phosphite esters, a variety of oxidants was examined but only (i) aqueous hydrogen peroxide and (ii) a solution of iodine buffered with bicarbonate were suitable. Oxidation of ethyldichlorophosphine was carried out in benzene containing sulphuryl chloride.

Analysis of Products.—In the hydrolysis reactions, the products were determined acidimetrically, and results agreed well with analyses on the original compounds, *i.e.*, reactions were >99% quantitative. For the oxidation reactions it was necessary to have the oxidant present in large excess and an accurate assessment of the amount consumed was impracticable; however, a check was made by means of separate non-calorimetric runs in which the ratio of sample to oxidant was greater, an increased time being allowed for completion of the reaction.

Heats of solution, and heats of neutralisation of acids where relevant, were determined in the same apparatus as used for the main investigation. Latent heats of vaporisation were estimated from vapour-pressure plots, except where published information on latent heat was already available.

Subsidiary thermochemical data used in deriving heats of formation ($\Delta H_f°$) and average bond energies were taken from National Bureau of Standards, Circular 500.

Estimates of Error.—Purely calorimetric errors have been assessed in the course of calibration; they are not greater than ±1·0%. Errors due to impurity in materials and to side reactions are probably less than 1% for the hydrolytic experiments but may be 2% in the oxidation studies. Latent heat estimates are in some cases very approximate but errors are unlikely to be greatly in excess of one kcal.

Results.—R = moles of solvent per mole of sample.

(a) *Hydrolysis of alkylphosphonic dichlorides in water*: $R·POCl_2 + 2H_2O(l.) \longrightarrow R·PO(OH)_2(aq.) + 2HCl(aq.)$.

(i) Me·$POCl_2$ (c.)						(ii) Et·$POCl_2$ (l.)					
Wt. (g.)	R	ΔH, obs. (kcal.)	Wt. (g.)	R	ΔH, obs. (kcal.)	Wt. (g.)	R	ΔH, obs. (kcal.)	Wt. (g.)	R	ΔH, obs. (kcal.)
0·7839	4700	−47·2	0·8191	4500	−47·1	0·6808	6000	−49·4	0·7730	5300	−49·6
0·6670	5500	−46·7	0·5751	6400	−46·9	0·5455	7500	−49·0	1·0795	3800	−49·5
				Mean	−47·0					Mean	−49·4

ΔH (soln.) Me·$PO(OH)_2$ = <0·1. ΔH (soln.) Et·$PO(OH)_2$ = <0·1.

Heats of formation of the halides cannot be derived directly from the above, but the data can be reduced to:

(i) $\Delta H_f°$Me·$POCl_2$(c.) − $\Delta H_f°$Me·$PO(OH)_2$ (c.) = 103·8 kcal./mole.

(ii) $\Delta H_f°$Et·$POCl_2$(l.) − $\Delta H_f°$Et·$PO(OH)_2$ (c.) = 106·2 kcal./mole.

(b) *Hydrolysis of* iso*propyl methylphosphonochloridate in water*: $(Pr^iO)MePOCl(l.) + H_2O(l.) \longrightarrow (Pr^iO)MePO·OH(aq.) + HCl(aq.)$.

Wt. (g.)	0·6047	0·6689	1·0260	0·6498	
R	7200	6500	4200	6700	
ΔH, obs. (kcal.)	−30·0	−29·3	−30·0	−28·7	Mean −29·5

ΔH (soln.) $(Pr^iO)MePO·OH$ = − 5·5 kcal.

$\Delta H_f°$ $(Pr^iO)MePO·Cl$ (l.) − $\Delta H_f°(Pr^iO)MePO·OH$ (l.) = 52·4 kcal.

(c) *Hydrolysis of diethyl phosphorofluoridate in aqueous sodium hydroxide* (0·5N): $(EtO)_2POF(l.) + 2NaOH(aq.) \longrightarrow (EtO)_2PO·ON·ONa(aq.) + NaF(aq.) + H_2O(l.)$.

Wt. (g.)	0·8400	0·8650	1·1857	1·2012	
R	5200	5100	3700	3600	
ΔH, obs. (kcal.)	−46·4	−46·1	−47·2	−46·9	Mean −46·6

Heat of reaction of diethyl hydrogen phosphate with aqueous NaOH = −22·0 kcal.

$\Delta H_f°(EtO)_2POF(l.) - \Delta H_f°(EtO)_2PO·OH(l.)$ = + 0·9 kcal.

(d) *Hydrolysis of tetraethyl pyrophosphate in aqueous sodium hydroxide* (0·5N): $(EtO)_2PO·O·PO(OEt)_2(l.) + 2NaOH(aq.) \longrightarrow 2(EtO)_2PO·ONa(aq.) + H_2O(l.)$.

Wt. (g.)	1·8975	1·5970	2·5271	1·9360	
R	4200	5000	3200	4100	
ΔH, obs. (kcal.)	−58·1	−58·1	−58·1	−58·6	Mean −58·2

$\Delta H_f°$ $(EtO)_2PO·O·PO(OEt)_2$ (l.) − $2\Delta H_f°$ $(EtO)_2PO·OH$ (l.) = 82·5 kcal.

(e) *Oxidation of* tri*isopropyl phosphite to phosphate with neutral aqueous hydrogen peroxide* (5%): $(Pr^iO)_3P(l.) + H_2O_2(aq.) \longrightarrow (Pr^iO)_3PO(aq.) + H_2O(l.)$.

Wt. (g.)	1·3022	0·8343	1·1167	
R	4400	6900	5200	
ΔH, obs. (kcal.)	−103·1	−104·5	−103·2	Mean −103·6

ΔH (soln.) $(Pr^iO)_3PO$ = − 3·6 kcal.

$\Delta H_f°$ $(Pr^iO)_3P$ (l.) − $\Delta H_f°$ $(Pr^iO)_3PO$ (l.) = 77·4 kcal.

(f) *Oxidation of ethyldichlorophosphine with sulphuryl chloride in benzene*: $EtPCl_2(l.) + SO_2Cl_2(benzene) \longrightarrow Et·POCl_2(benzene) + SOCl_2(benzene)$.

Wt. (g.)	0·9855	0·8877	0·6384	0·7413	
R	750	840	1160	1000	
ΔH, obs. (kcal.)	−40·8	−40·1	−40·7	−40·9	Mean −40·6

ΔH (soln.) Et·$POCl_2$ in benzene = < 0·1 kcal.

ΔH (soln.) SO_2Cl_2 in benzene = < 0·1 kcal.

ΔH (soln.) $SOCl_2$ in benzene = − 0·6 kcal.

Using the values for $\Delta H_f°SOCl_2$ and $\Delta H_f°SO_2Cl_2$ given in *J.*, 1954, 2156, we get: $\Delta H_f°EtPCl_2(l.) - \Delta H_f°Et{\cdot}POCl_2(l.) = 74{\cdot}8$ kcal.

(g) *Oxidation of diethyl hydrogen phosphite with iodine in the presence of bicarbonate*:

$$(EtO)_2P{\cdot}OH(l.) + KI_3(aq.) + 3KHCO_3(aq.) \longrightarrow (EtO)_2PO{\cdot}OK(aq.) + 3KI(aq.) + 3CO_2(aq.) + 2H_2O(l.)$$

Wt. (g.)	1·1464	0·7065	0·9133	0·9160	
R	3300	5500	4200	4200	
ΔH, obs. (kcal.)	−56·7	−57·2	−57·4	−56·7	Mean −57·0

Heat of reaction of diethyl hydrogen phosphate with aqueous KOH: −22·4 kcal./mole.

$\Delta H_r°(EtO)_2P{\cdot}OH(l.) - \Delta H_f°(EtO)_2PO{\cdot}OH(l.) = 81{\cdot}5$ kcal.

Discussion

Although it is not possible to derive heats of formation directly from the data recorded above, the information is useful in permitting the computation of "average bond-energy" terms from which heats of formation can be estimated when used in conjunction with similar data on other phosphorus bonds (to be reported in a subsequent paper). Ideally such quantities should be derived from the heats of formation of molecules containing only one type of bond PX_n, when

$$\bar{D}(P{-}X) = Q_f(a)PX_n/n$$

where $Q_f(a)PX_n$ is the heat of formation of the compound in the gaseous state from normal gaseous atoms. For tervalent phosphorus such data are available in the case of the halides and phosphine:

$\bar{D}$(P–F) 117 kcal.[1] $\bar{D}$(P–Cl) 76·3 kcal.[2] $\bar{D}$(P–Br) 61·7 kcal.[3] $\bar{D}$(P–H) 76·3 kcal.[4]

[1] Berthelot, *Ann. Chim. Phys.*, 1885, **6**, 358. [2] Neale and Williams, *J.*, 1954, 2156. [3] Charnley and Skinner, *J.*, 1953, 450; Neale and Williams, *loc. cit.* [4] Nat. Bur. Stand., Circular 500 (1952).

A compound such as phosphorus pentachloride does not afford similar information for quinquevalent phosphorus, as the polar and equatorial bonds are known to differ (cf. bond lengths) and in any case its structure (trigonal bipyramid) is such that data obtained from it could not be applied to compounds containing the phosphoryl (P=O) bond, which have a tetrahedral structure. The first step in deriving average bond-energy terms for quinquevalent organic phosphorus compounds is therefore to determine the quantity to be allowed for the phosphoryl bond.

Estimates of bond energy in the P=O bond, based on thermochemical measurements involving the formation of the latter, must necessarily be empirical, as they embody not only the valency promotion energy but also any change resulting from strengthening of other bonds in the molecule. Since the bonds in tervalent phosphorus compounds are probably formed from the *p* orbitals, and those in the phosphoryl compounds from hybridised orbitals, the latter would be expected to be the stronger. A number of estimates of the phosphoryl bond energy are possible both from previously published data and from those recorded above; in all cases the phosphoryl compound is compared directly with the corresponding tervalent compound:

Basis of estimate	D(P=O) (kcal.)	Source of information
$\Delta H_f°$ P_4O_6 and P_4O_{10}	115	Koerner and Daniels, *J. Chem. Phys.*, 1952, **20**, 113, and private communication
$\Delta H_f°$ PCl_3 and $POCl_3$	127·5	Neale and Williams, *J.*, 1952, 4535; 1954, 2156
ΔH oxidation of PF_3	129·8	Ebel and Bretscher, *Helv. Chim. Acta*, 1929, **12**, 450
ΔH oxidation of $(Pr^iO)_3P$	134·1	Present paper, (*e*) above
ΔH oxidation of $EtPCl_2$	131·0	Present paper, (*f*) above

More recently Skinner (private communication) has determined the heat of oxidation of triethyl phosphite with hydrogen peroxide in ethanol; his results indicate a value exceeding 140 kcal. for D(P=O). Although the phosphoryl bond energy probably varies to some

extent, it is evident from bond-length data in the case of phosphorus halides that the effect is partly due to strengthening of the P–Cl bond :

	PCl_3 [a]	$POCl_3$ [b]
P–Cl	2·04 Å	1·99 Å

[a] Kisliuk and Townes, *Phys. Rev.*, 1950, **78**, 347. [b] Williams, Gordy, and Sheridan, *J. Chem. Phys.*, 1952, **20**, 164.

Although similar bond-length data are not available for the phosphorus esters, it seems likely that the effect is even more marked and in a subsequent paper we shall present evidence, based on the heats of esterification of PCl_3 and $R{\cdot}POCl_2$ type compounds, which indicates that the P–OR link in quinquevalent compounds is appreciably stronger than in tervalent compounds.

For the practical purpose of setting up a table of average bond-energy terms, however, it is legitimate to regard D(P=O) as constant provided that the experimental data involve only reactions of phosphoryl compounds. In effect this necessitates independent assessments of bond-energy terms for (i) tervalent phosphorus compounds and (ii) quinquevalent (phosphoryl) compounds. The following estimates are made on the assumption of a constant minimum value of D(P=O) = 115 kcal. The only justification for adopting this figure (apart from the evidence of Koerner and Daniels) is that bond-length measurements on the phosphorus halides suggest a strengthening of the P–X link in POX_3 as compared with PX_3; if this is so, direct comparison of the heats of formation of phosphorus and phosphoryl halides will give values for D(P=O) which are too high.

The method of deriving the bond-energy terms presents no novelty; it will be self-evident from the example given below the table.

Heat of formation data used	Heat of vaporn. or sublimn. (kcal.)	Reference	Average bond-energy in the phosphoryl molecule (kcal.)	
$POCl_3$	9·5	Neale & Williams, *J.*, 1952, 4535	$\bar{D}$(P–Cl)	80
$POBr_3$	15·0	Charnley & Skinner, *J.*, 1953, 450	$\bar{D}$(P–Br)	65
$Me{\cdot}POCl_2$–	14·9	Present paper	$\bar{D}$(P–OH)	105
$Me{\cdot}PO(OH)_2$	11·5	(a) (i) above		
$Et{\cdot}POCl_2$–	10·2	Present paper,	$\bar{D}$(P–OH)	104
$Et{\cdot}PO(OH)_2$	12·1	(a) (ii) above		
$(Pr^iO)MePO{\cdot}Cl$–	14·0	Present paper,	$\bar{D}$(P–OH)	104
$(Pr^iO)MePO{\cdot}OH$	14·5	(b) above		
$(EtO)_2POF$–	11·0	Present paper,	$\bar{D}$(P–F)	120
$(EtO)_2PO{\cdot}OH$	10·0	(c) above		
$(EtO)_2PO{\cdot}O{\cdot}PO(OEt)_2$–	13·1	Present paper,	$\bar{D}$(P–OP)	96
$2(EtO)_2PO{\cdot}OH$	10·0	(d) above		
P_4O_{10}	17·6	Roth, Meichsner, & Richter, *Arch. Eisenhuttenw.*, 1934, **8**, 239	$\bar{D}$(P–OP)	95
$(EtO)_2P{\cdot}OH$–	7·0	Present paper,	$\bar{D}$(P–H)	78
$(EtO)_2PO{\cdot}OH$	10·0	(g) above		

Example :

$$\Delta H_f^\circ Me{\cdot}POCl_2(c.) - \Delta H_f^\circ Me{\cdot}PO(OH)_2(c.) = 103{\cdot}8 \text{ kcal.}$$

or
$$Q_f Me{\cdot}PO(OH)_2(c.) - Q_f Me{\cdot}POCl_2(c.) = 103{\cdot}8 \text{ ,,}$$

in the gaseous phase :

$$Q_f Me{\cdot}PO(OH)_2(g.) - Q_f Me{\cdot}POCl_2(g.) = 107{\cdot}2 \text{ ,,}$$

from atoms :

$$Q_f(a)Me{\cdot}PO(OH)_2 - Q_f(a)Me{\cdot}POCl_2 = 271{\cdot}6 \text{ ,,}$$

Putting k for the heat of formation from atoms of that part of the molecule common to both, we have

$$Q_f(a)Me{\cdot}PO(OH)_2 = k + 2(P–OH) + 2(O–H)$$

$$Q_f(a)Me{\cdot}POCl_2 = k + 2(P–Cl)$$

and $$Q_f(a)Me{\cdot}PO(OH)_2(a) - Q_f(a)Me{\cdot}POCl_2 = 2(P–OH) + (2 \times 110{\cdot}5) - (2 \times 80{\cdot}0)$$

Therefore $271{\cdot}6 = 2(P–OH) + 61{\cdot}0$ and $\bar{D}(P–OH) = \frac{1}{2}(271{\cdot}6 - 61{\cdot}0) = 105{\cdot}3$ kcal.

The authors thank Messrs. A. H. Ford-Moore and A. F. Childs for the preparation and purification of compounds, and Miss M. Howells for assistance in the calorimetry and analysis. Helpful discussions with Dr. H. A. Skinner (Manchester University), Professor E. C. Baughan (Royal Military College of Science), and Mr. B. Topley (Messrs. Albright and Wilson) are also gratefully acknowledged, as also is permission to publish this work, given by the Chief Scientist, Ministry of Supply.

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The Catalytic Hydrogenation of Ethylene at a Nickel Surface. Part I. The Chemisorption of Ethylene.

By G. I. JENKINS and SIR ERIC RIDEAL.

[Reprint Order No. 6115.]

The adsorption of ethylene and hydrogen on nickel films has been examined. The ethylene undergoes dissociative chemisorption to form an adsorbed acetylenic complex and two chemisorbed hydrogen atoms, requiring four contiguous sites for the process. Gaseous ethylene can rapidly remove the chemisorbed hydrogen and where four contiguous vacancies are formed ethylene in its turn is chemisorbed with dissociation. The final structure on admission of the two gases is some 80% coverage by acetylenic complexes, 10% by hydrogen on double sites, and 10% on single sites. This distribution is confirmed by pictorial filling of squares of 100 sites. The chemisorbed hydrogen on the 10% of double sites on this covered surface is readily removed by ethylene to form ethane. No evidence of chemisorbed ethylene was found.

IN spite of the interest which has been devoted to this classical heterogeneous reaction since its discovery by Sabatier, the detailed mechanism of its operation is not yet established. Excellent reviews of the various mechanisms proposed have been written by Eley (*Quart. Reviews*, **1949**, **3**, 209), Laidler (" Catalysis," Reinhold Publishing Corporation, New York, **1954**, Vol. I, p. 168), and Eyring, Parlin, Wallenstein, and Zwolinski (" General Theories of Heterogeneous Catalysis," **1953**, Technical Report XI, 69), as well as that presented in the Faraday discussion on heterogeneous catalysis held in **1950** (Vol. **8**).

There appears to be general agreement that the reaction proceeds through an " associative " adsorption of ethylene, a divergence of opinion existing on whether the subsequent reaction proceeds by the so-called Langmuir–Hinshelwood mechanism with adsorbed hydrogen (Farkas, Farkas, and Rideal, *Proc. Roy. Soc.*, **1934**, *A*, **146**, 630; Horiuti, Ogden, and Polanyi, *Trans. Faraday Soc.*, **1934**, **30**, 663, 1164), or by the alternative mechanism of reaction with gas-phase or van der Waals-adsorbed hydrogen (Rideal, *Proc. Camb. Phil. Soc.*, **1939**, **35**, 130; Rideal and Twigg, *Proc. Roy. Soc.*, **1939**, *A*, **171**, 55). The " associative " adsorption of ethylene may be formulated

$$C_2H_4 + 2Ni \longrightarrow \begin{matrix} CH_2\text{–}CH_2 \\ Ni \qquad Ni \end{matrix} \quad \ldots\ldots\ldots (1)$$

From studies of the exchange reaction with deuterium, it has been concluded that a " dissociative " adsorption of ethylene can also occur (Farkas, Farkas, and Rideal, *loc. cit.*):

$$C_2H_4 + 2Ni \longrightarrow C_2H_3Ni + NiH \quad \ldots\ldots\ldots (2)$$

Evidence that a " dissociative " adsorption does occur in nickel was first presented by Sabatier (" La Catalyse en Chimie Organique," Lib. Polytechnic, Paris) who records a carbonisation of the catalyst in the presence of ethylene at 300°. Later workers (Beeck, *Rev. Mod. Phys.*, **1945**, **17**, 61; Morikawa, Trenner, and Taylor, *J. Amer. Chem. Soc.*, **1937**, **59**, 1103; Douglas and Rabinovitch, *ibid.*, **1952**, **74**, 2486) found that on admission of

ethylene at lower temperatures a self-hydrogenating reaction occurs, ethane being produced.

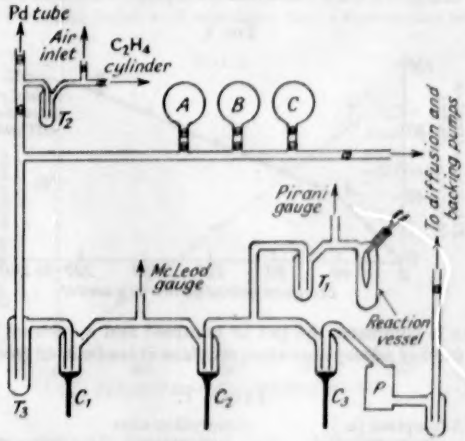
Beeck, Smith, and Wheeler (*Proc. Roy. Soc.*, 1940, *A*, **177**, 62) concluded on somewhat slender evidence that the ethylene was adsorbed on four sites (the ratio of hydrogen to ethylene adsorbed being 2 : 1). When later they observed a decomposition of ethylene, the mechanism of adsorption postulated was

$$C_2H_4 + 4Ni \longrightarrow \underset{Ni \quad\quad Ni}{\overset{CH=CH}{\diagup\!\diagdown}} + 2NiH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

In this computation, however, it was overlooked that the ethylene adsorption on which the ratio was based fails to take into account the fact that the ethane found in the gas phase must have received its hydrogen from the surface, thus rendering more surface available for further ethylene addition.

Separate experiments revealed that the addition of ethylene to a hydrogen-covered surface results in a rapid reaction, ethane appearing in the gas phase.

FIG. 1.



To explain the kinetics of the hydrogenation reaction, Beeck (*Discuss. Faraday Soc.*, 1950, **8**, 118) assumed that some ethylene was also adsorbed " associatively " on that part of the surface not covered with the dehydrogenated complexes formed by (3) but no direct experimental evidence was advanced to support this view.

The carbonisation reaction which Sabatier showed took place at 300° can be formulated as a sequel to (3) :

$$\underset{Ni \quad\quad Ni}{\overset{CH=CH}{\diagup\!\diagdown}} \longrightarrow \underset{Ni \quad\quad Ni}{\overset{C-C}{\diagup\!\diagdown}} + 2NiH \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Much is known about the behaviour of hydrogen when brought into contact with nickel (Beeck, *Adv. in Catalysis*, 1950, **2**, 151 ; De Boer and Schuit, *Rec. Trav. chim.*, 1953, **72**, 909). In view of the apparent complexity of the ethylene reactions it appeared desirable, before dealing with the actual hydrogenation process, to examine in somewhat more detail the sequence of events when ethylene is brought into contact with nickel. The actual state of the surface when the catalytic reaction is proceeding at a steady rate must be dependent on the result of these reactions. A knowledge of the surface state during hydrogenation, together with data on the kinetics of the process, should assist in revealing the molecular mechanism.

EXPERIMENTAL

Clean and reproducible nickel surfaces were obtained by evaporation of a hairpin filament of spectroscopically pure nickel (26 s.w.g.) spot-welded to tungsten–Pyrex seals. Reaction

vessels of 30 ml. capacity, coated internally with the freshly evaporated nickel films, were employed. A Pirani gauge was attached to the reaction vessel and connected through traps and mercury cut-offs to the McLeod gauge, diffusion and backing pumps, hydrogen and ethylene dosers, and gas-storage vessels in the customary manner, as shown in Fig. 1.

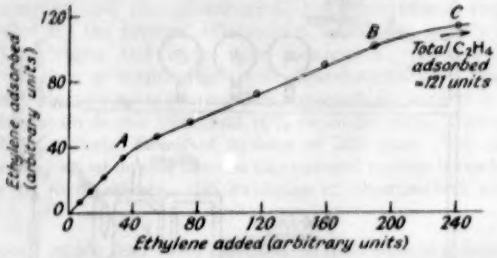
Hydrogen was prepared from cylinder gas by diffusion through a palladium tube, and ethylene by repeated fractionation of the liquefied gas from a cylinder. To minimise the introduction of impurities from the Pyrex glass reservoirs and tubing, prolonged heating under high vacuum was frequently carried out, and no gas sample was retained for more than 24 hr. in the reservoirs.

The quantities of gas adsorbed or desorbed are given in units corresponding to a pressure change of $1{\cdot}00 \times 10^{-3}$ mm. Hg (*i.e.*, $9{\cdot}6 \times 10^{15}$ molecules).

Gas mixtures were analysed by fractional condensation at low temperatures.

Results.—(a) *Complex formation.* When increments of ethylene are admitted to a clean film at 20° two distinct phases are to be observed (Fig. 2). The first few increments (*O*—*A*) are completely chemisorbed with extreme rapidity. On further addition (*ABC*) more gas is rapidly adsorbed but there is now a concordant rise in the residual gas pressure on each admission. Analysis of the residual gas revealed that it was practically pure ethane up to the point *B*; beyond this point both ethane and ethylene were found in the gas phase.

FIG. 2.



If, when adsorption is complete, the gas be removed and a vacuum maintained for 30 min. there is practically no further adsorption when ethylene is readmitted (see Table 1).

TABLE 1.

Catalyst	Adsorption in phase (ii)	Adsorption after evacuation	Adsorption after repeating evacuation
A_1	65	2·0	0·5
B_1	110	1·0	nil

At the end of phase (i) the volume of ethylene adsorbed is approximately only one-quarter of the amount of hydrogen adsorbed irreversibly at −183° on films of the same area. This ratio was found to be independent of the film thickness, indicating that there is no solution of hydrogen in the metal at −183° during the course of the experiments. The data are given in Table 2.

TABLE 2.

	C_2H_4 adsorbed:			
Catalyst	Phase (i)	Phase (ii)	Catalyst	Irreversible H_2 adsorption at −183°
A_1	37	65	A_2	150
B_1	68	110	B_2	253
C_1	84	—	C_2	290
D_1	41	80	D_2	145

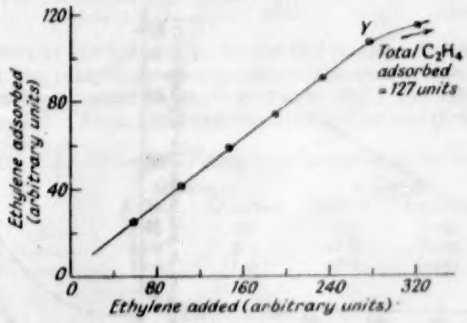
Since molecular hydrogen is chemisorbed to occupy two lattice points, if the surface were completely covered at the end of phase (i) the chemisorbed ethylene would have to occupy at least 8 points. This is highly improbable and we must conclude that a considerable fraction of the surface is bare when the second phase commences. That there are in fact bare sites at the end of phase (i) was confirmed by cooling from 20° to −78° and adding hydrogen, when a marked instantaneous irreversible adsorption occurs. Thus on one catalyst where 84 units of ethylene had been adsorbed in phase (i), no less than 46 units of hydrogen were taken up

irreversibly. Trapnell (*Trans. Faraday Soc.*, 1952, **48**, 160), who observed a similar phenomenon on tungsten films, suggested that the second phase commences when the hydrogen bonding to the catalyst weakens and a detectable quantity of hydrogen appears in the gas phase. The large irreversible adsorption of hydrogen at −78° which we observe, however, shows that this is not so in the case of nickel. Instead, it would appear that as a result of the rapid fall in the heat of adsorption of ethylene on nickel (Beeck, *loc. cit.*, 1945) the reaction of gas-phase ethylene with adsorbed hydrogen becomes energetically more favourable than the adsorption of ethylene before the surface is filled. Removal of hydrogen then increases the available area for adsorption, this process constituting phase (ii) of the isotherm.

A reaction of gas-phase ethylene with adsorbed hydrogen has been postulated. That such a reaction occurs was shown by Beeck (*loc. cit.*, 1945), and this has been carefully studied in this series of experiments by adding ethylene in successive increments to a hydrogen-covered surface at 20° (Fig. 3). The residual gas was found to be entirely ethane up to a point *Y*. The resemblance of the slopes (ethylene adsorbed/ethylene added) for the reaction of gas-phase ethylene with its own decomposition product on the nickel surface [phase (ii) in the adsorption of ethylene], and the reaction of gas-phase ethylene with hydrogen adsorbed on the surface is at once apparent (Figs. 2 and 3 respectively).

We have seen that at the end of phase (ii) dehydrogenated ethylene residues are present. The surface in this state cannot react with ethylene, and experiments were carried out to see

FIG. 3.



whether any reaction occurred with gaseous hydrogen. Ethylene was added to a clean nickel film at 20° until no further gas was adsorbed. Readmission of ethylene after evacuation for 30 min. resulted in no further adsorption. On further evacuation for 30 min. and addition of a known amount of hydrogen, an instantaneous decrease in pressure was observed, followed by a slow continuous pressure decrease. This slow reaction proceeds at a speed comparable to that observed by Beeck (*loc. cit.*, 1945), who found that hydrogen took 1 hr. to remove 20% of the complexes from a nickel film at 20°, the product consisting of 90% saturated hydrocarbon polymers (C_4—C_8) and 10% ethane. However, in our experiments ethane only was formed, hydrogen being subsequently adsorbed on the sites vacated by the saturated hydrocarbon. The initial rate of this slow reaction was found to be proportional to the initial hydrogen gas pressure (Fig. 4).

The instantaneous fall of pressure observed on admitting the hydrogen might be due either to the hydrogenation of some chemisorbed ethylene adsorbed on two sites (associative adsorption) followed by adsorption of hydrogen on the vacated sites, or to adsorption of hydrogen on bare sites inaccessible to ethylene. That the latter was the case was confirmed by the following experiments. Instead of allowing the slow hydrogenation of the complexes to proceed, the reaction vessel was pumped out for 30 min. Readmission of hydrogen resulted in a similar instantaneous adsorption but no adsorption of ethylene occurred if that gas was admitted. Thus, on a complex-covered surface, there is a reversible adsorption of hydrogen but no adsorption of ethylene.

In agreement with Beeck's conclusions, though not with the evidence with which he supported them, the surface complexes were found to correspond to an acetylenic complex in composition; thus in one experiment, 121 units of ethylene were adsorbed and a further 120

units of gaseous ethylene were converted into ethane. We have seen that this complex-covered surface has bare sites which are accessible for the chemisorption of hydrogen. An approximate value for the capacity of the surface, as measured by the low-temperature irreversible hydrogen adsorption, was found to be 145 units or 290 sites. It is probable that each C_2H_2 complex occupies two sites; the 121 units would thus leave 48 sites bare. It was found that 12 units of hydrogen could be adsorbed on the complex-covered surface, *i.e.*, on the bare 48 sites. It would therefore appear that of these 48 bare sites, 24 are in pairs accessible to hydrogen and 24 are isolated single sites accessible presumably only to atomic hydrogen by diffusion through the metal substrate.

We thus derive the following picture of a catalyst surface in the presence of a hydrogen ethylene gas mixture:

Sites:	occupied by C_2H_2 complexes	occupied by hydrogen as pairs	unoccupied
	242	24	24
	83·4%	8·3%	8·3%

Following the method of Roberts ("Some Problems in Adsorption," Cambridge Univ. Press, 1939) and of Herington and Rideal (*Trans. Faraday Soc.*, 1944, **40**, 505) a pictorial representation of the surface can be made by taking 100 sites, surrounded by a suitable guard ring to eliminate end effects, and filling these in a haphazard manner with ethylene in such a way that each molecule requires four free contiguous sites for adsorption. Once the pattern has been filled

FIG. 4.

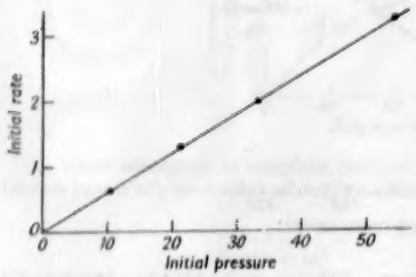
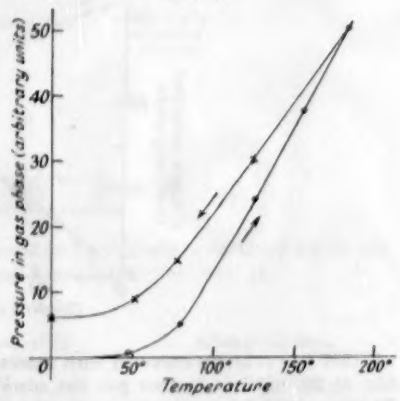


FIG. 5.



in this manner hydrogen pairs are removed and the vacancies caused by this removal are in their turn filled with ethylene in those places where four contiguous sites are formed by the removal of the hydrogen. This process is continued until the pattern is completed; the results obtained are:

C_2H_2 complexes, 78% H_2 as pairs, 13% Single, 9%

The agreement with the experimentally derived distribution is satisfactory.

(b) *Thermal stability of the complex.* The surface complex formed on reaction with ethylene is, as we have seen, an acetylenic one ($Ni_2C_2H_2$). Sabatier noted that at 300° carbonisation occurred and we can infer that this carbide is produced by further dehydrogenation.

When a complex-covered nickel catalyst is heated to 170°, gas, identified as practically all hydrogen, is evolved as indicated in the following analysis. Thus the decomposition of the complex to carbide appears to be almost complete at 170°. On cooling, the hydrogen can be readsorbed on the surface (Fig. 5) and the process is reversible.

Catalyst	Surface complexes	Hydrogen desorbed	Catalyst	Surface complexes	Hydrogen desorbed	Catalyst	Surface complexes	Hydrogen desorbed
K_1	60	50	K_2	28	22	K_3	14	11

This adsorption of hydrogen on cooling means that either (i) it can react reversibly with the surface carbide to form acetylenic complexes or (ii) some of the surface carbide has migrated into the interior of the metal, leaving a fresh nickel surface for the hydrogen.

If the former view be correct, addition of hydrogen at 20° after heating should result in a hydrogenation reaction. This reaction does not occur however (Table 3, reactions 1 and 2).

TABLE 3.—28 *Complexes on the surface.*

Pre-treatment	Hydrogen added	Pressure after : ¼ min.	6 min.	12 min.
Complex-covered surface :				
(1) before heating (acetylenic surface)	60·9	53·5	40·7	36·3
(2) after heating (carbide surface)	60·2	55·0	53·5	53·4
(3) addition of C_2H_4	55·2	49·3	42·0	40·6

If migration has occurred there should be an appreciable quantity of hydrogen adsorbed at 20°. Addition of ethylene should then result, as we have seen previously, in an adsorption with ratio (ethylene adsorbed)/(ethylene added) of 0·4. That this is in fact the case was shown in a number of experiments. Furthermore, this surface having been treated with ethylene, the complexes reacted with hydrogen as expected (Table 3, reaction 3).

Solution of the carbide at 170° was finally established by adding large increments of ethylene (38·2 units followed by 36·1 units) to a surface previously saturated at 20° with 14 units of complexes. The surface remained active for the decomposition, the hydrogen being disengaged at the following rate :

	Pressure recorded after (min.)			
Ethylene added	¼	4	8	60
31·6 units	47·3	57·5	59·8	60·5

(c) *Adsorption of ethylene and hydrogen on the carbided surface.* Hydrogen but no ethylene or ethane is adsorbed on the complex-covered surface. The surface was carbided by heating it to 170° for 30 min. in the presence of ethylene (5 mm. Hg). The ethylene was pumped out and the catalyst was cooled. Again hydrogen was adsorbed but no ethylene or ethane (Table 4).

TABLE 4.—*Number of complexes adsorbed = 50 units.*

Surface	Hydrogen Added	Hydrogen Adsorbed	Ethylene Added	Ethylene Adsorbed	Ethane Added	Ethane Adsorbed
Complex-covered (20°)	13·4	6·5	35·5	None	30·0	None
Carbide-covered (20°)	13·0	2·5	47·8	None	31·2	None
Carbide-covered (170°)	14·0	1·0	46·0	None	—	—

DISCUSSION

These adsorption studies show that in fact "associative" adsorptiom does not occur. On the contrary, we find that (1) ethylene on chemisorption is dissociated to an acetylenic complex and chemisorbed hydrogen and (2) there is no reversible adsorptiom of ethylene in the isotherm. (3) Any small quantity of ethylene adsorbed by two-site contact should react quickly with hydrogen, leaving sites available for an equivalent readsorption of ethylene. No such readsorptiom occurs.

This applies to the complex-covered surface. When the surface has been heated and the complex has lost its hydrogen and become carbided, again no adsorption of ethylene is observed. In view of this, two mechanisms seem possible in the formation of ethane from ethylene.

(a) *Hydrogenation of the complexes.* Assuming that the first-order dependence of this reaction (Fig. 4) holds at an initial pressure of 5 cm. of hydrogen, 4×10^{-3} cm. of ethane would be produced in 5 min. (500 c.c. volume). In the same volume and with a similar film area the hydrogenation reaction using 5 cm. of hydrogen and ethylene goes to completion in under 5 min. This factor is thus only of secondary importance in the hydrogenation reaction.

(b) *Adsorption of hydrogen followed by reaction with gas-phase ethylene.* It has been observed that an adsorption of hydrogen does occur on both complex and carbided surfaces. Also, that the reaction of adsorbed hydrogen with gaseous ethylene occurs rapidly. It might be concluded that the hydrogenation of ethylene occurs by a Rideal-type mechanism, gas-phase ethylene reacting with hydrogen adsorbed on vacant sites on a complex-covered surface producing ethane, more hydrogen then being adsorbed.

Indeed, this type of mechanism involving the reaction between a chemisorbed and a van der Waals or gas-phase species, seems to be general in this system since, as we have seen, the chemisorbed complexes can co-exist with chemisorbed hydrogen on the surface and are only hydrogenated by an excess of hydrogen in the gas phase.

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CHEMISTRY DEPARTMENT,
UNIVERSITY OF LONDON, KING'S COLLEGE. [*Received, February 9th*, 1955.]

The Catalytic Hydrogenation of Ethylene at a Nickel Surface. Part II. The Reaction Mechanism.*

By G. I. JENKINS and SIR ERIC RIDEAL.

[Reprint Order No. 6116.]

The evidence for the mechanism of the hydrogenation of ethylene on nickel advanced in Part I is supported by experiments on nickel films which have been pre-treated to form respectively partly complex-covered and partly "carbided" surfaces. The formal reaction kinetics over a wide range of temperatures and partial pressures of the reacting gases are likewise found to be in conformity with the mechanism proposed.

IN Part I * it was shown by measurement of gas adsorption on nickel films that when the metal is exposed to ethylene gas the surface becomes progressively covered with acetylenic residues until some 80% of the surface is so covered. In the presence of hydrogen a further 10% of the complex-covered surface can adsorb hydrogen, whilst the residual 10% consists presumably of isolated sites which may be covered with hydrogen atoms by migratory processes within the metal. Further, the hydrogen thus adsorbed is readily removed by gaseous ethylene to form ethane. No evidence of the presence of chemisorbed ethylene as such was found.

We might infer that during active catalysis this hydrogen-accessible 10% of the surface alone is the operative area, since the slow rehydrogenation of the surface complexes has been found to furnish but a minor contribution, the main reaction consisting of the chemisorption of hydrogen and its removal by gaseous ethylene to form ethane.

Any completely satisfactory scheme for the molecular mechanism must permit us to interpret the following experimental facts on which there appears to be general agreement: (1) Over the temperature range investigated the reaction velocity is proportional to the pressure of hydrogen gas. (2) According to the detailed studies of zur Strassen (*Z. physikal. Chem.*, 1934, *A*, **169**, 81) and Toyama (*Rev. Phys. Chem. Japan*, 1937, **11**, 153; 1938, **12**, 115) the rate is proportional to the ethylene pressure at high temperatures and independent thereof at room temperatures. (3) A maximum is observed in the rate–temperature curve, and this maximum appears to move to higher temperatures with increasing ethylene pressures (Rideal, *J.*, 1922, **121**, 309; Melville, *J.*, 1934, 803; zur Strassen, *loc. cit.*). (4) Admission of ethylene at 20° results in a self-hydrogenating reaction and an acetylenic complex is left on the surface. At higher temperatures this complex can be converted into carbide as first shown by Sabatier. (5) Ethane does not influence the reaction (Rideal, Toyama, Beeck). (6) There is in addition an exchange reaction with deuterium and a migration of the double bond in such olefins as butene.

A number of investigators have commenced their studies with clean nickel wires or films. We would expect that the reactivity of a nickel surface would be initially high, falling to a constant value as the ethylene complex builds up to its final stationary coverage. In many systems diffusion processes may limit the rate of reaction and it was considered important to investigate these two points in some detail as well as confirm the kinetics which the majority of investigators have found.

* Part I, preceding paper.

Experimental

Preliminary work with the small reaction vessel (30 c.c. volume with a 50-mg. metal film, cf. Part I, *loc. cit.*) showed that even at 20° the effects of gas diffusion on the reaction velocity were considerable (*i.e.*, no appreciable increase in rate on increasing the temperature). Since this involved diffusion of reactant gases from the connecting tubes, a magnetically driven glass centrifugal pump was introduced into the circuit. As seen in Fig. 1, the rate of hydrogenation in a mixture of hydrogen and ethylene (5·6 cm. pressure of each gas) was found to be dependent on the speed of the pump. This offers an explanation for the results obtained by Palmer and Palmer (*Proc. Roy. Soc.*, **1921**, *A*, **99**, 402). The reaction system was accordingly redesigned so that no dead space was present and a smaller weight of nickel evaporated.

Commencing with a fresh catalyst a reaction mixture of the two gases in equal proportions was added (4·0 cm. pressure), and the rate of reaction determined for 10 min. at 20°. The

Fig. 1.

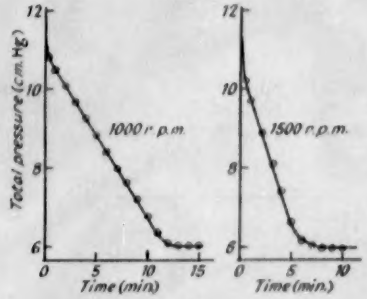
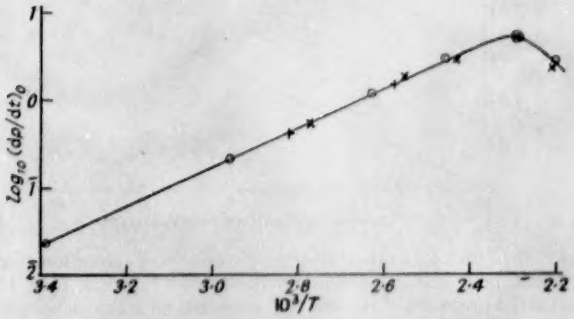


Fig. 2.



gases were then removed, and a fresh gas mixture admitted. The initial rates of reaction were found to be as in Table 1*a*. In every experiment the velocity of reaction reached a constant and reproducible value after one or two runs, the first being more rapid.

Table 1.

	(*a*) *With a fresh catalyst*					(*b*) *With a catalyst pre-treated with ethylene*		
Run No.	1	2	3	4	5	1	2	3
Rate (mm. Hg/min.)	3·50	1·90	1·30	1·30	1·30	1·60	1·30	1·40

In a further series of experiments the nickel catalyst was first exposed to ethylene gas at 4·0 cm. pressure for 30 min. at 20° before examining it for catalytic activity. This treatment, as expected, almost eliminated the initial fast reaction (Table 1*b*). The catalytic activity of a complex-covered surface was compared with that of a " carbided " surface formed by heating a complex-covered catalyst. The hydrogen adsorption on these two catalysts at 5×10^{-3} mm. pressure and 20° was 6·5 and 2·5 units respectively, whilst the rates of hydrogenation of ethylene at 4·0 cm. pressure and 20° were 0·60 mm./min. and 0·20 mm./min. respectively.

The close connection between the hydrogen adsorption and rate of reaction receives further

support from the results of experiments in which minute amounts of oxygen were admitted to the gas mixture. Rideal (*J.*, 1922, **121**, 309) showed that traces of oxygen in the gas mixture cause an induction period in the reaction during which the oxygen is preferentially hydrogenated to water. At 20°, in the presence of traces of oxygen, the induction period was found to be 240 sec. on a complex-covered catalyst and 600 sec. on a carbided catalyst, whilst the ratio of the active quantities of hydrogen adsorbed was 6·5 to 2·5.

Nickel films which had been exposed to ethylene for 30 min. at 190° were found to be very reproducible in behaviour.

The surface having been carbided, runs were made with the gases in equal proportions at 5 cm. Hg partial pressure over the range 20—180°. In Fig. 2 are given the details of runs on three different catalysts of different areas (after correction for the area) which have been

FIG. 3.

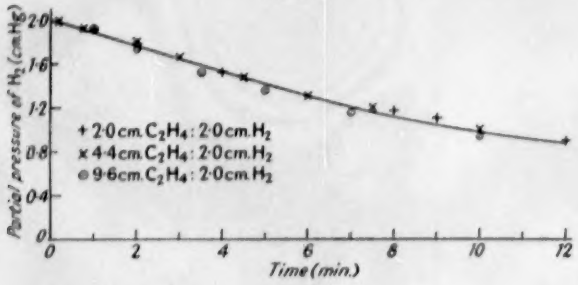
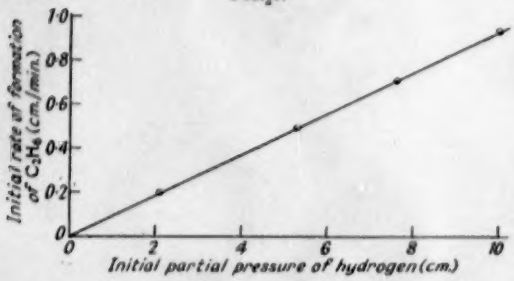


FIG. 4.



treated in this way. In accord with other workers, the energy of activation at low temperatures is found to be 10·2 kcal./mole and there is an inversion temperature at 160—165°.

On varying the partial pressures of the reacting gases the initial rates were found to conform to the relationship

$$(T_{165°})\ \text{Rate} = AP_{H_2}P_{C_2H_4}/(1 + BP_{C_2H_4})$$

The extent of agreement between experimental and calculated rates is given in Table 2. Below the inversion temperature the rate of reaction was independent of the ethylene pressure when that was varied from 2·0 to 9·6 cm. pressure but was directly proportional to the pressure of hydrogen as shown in Figs. 3 and 4.

Thus $(T_{114°0})\ \text{Rate} = KP_{H_2}$.

TABLE 2.

Initial pressures (cm. Hg)		Initial rates at 165° (mm./min.)		Initial pressures (cm. Hg)		Initial rates at 168° (mm./min.)	
C_2H_4	H_2	obs.	calc.	C_2H_4	H_2	obs.	calc.
2·1	1·9	0·7	0·9	2·1	1·9	0·7	0·9
5·0	2·0	1·3	1·5	3·0	5·3	3·0	3·3
9·8	2·0	1·9	1·9	2·8	9·8	6·0	6·0
3·0	5·3	3·0	3·3	5·0	2·0	1·3	1·5
5·2	5·3	4·5	4·2	5·2	5·3	4·5	4·2
10·6	4·8	4·4	4·6	4·8	10·4	9·0	8·1

Discussion

The comparative kinetics on complex-covered and "carbided" surfaces evidently supports the experimental evidence given in Part I (*loc. cit.*) in favour of the view that gaseous ethylene reacts with hydrogen chemisorbed on paired sites which occupy only some 10% of the surface of the nickel catalyst. If θ denotes the fraction of paired sites on which hydrogen is chemisorbed, we can write for the rate of chemisorption of hydrogen $k_1P_{H_2}(1 - \theta)$. The chemisorbed hydrogen can either evaporate at a rate $k_2\theta$ or react with gaseous ethylene at a rate $k_3P_{C_2H_4}\theta$. Under steady-state conditions

$$k_1P_{H_2}(1 - \theta) = k_2\theta + k_3P_{C_2H_4}\theta$$

Hence the rate of hydrogenation will be

$$k_3P_{C_2H_4}\theta = \frac{k_1k_3P_{H_2}P_{C_2H_4}}{k_2 + k_3P_{C_2H_4} + k_1P_{H_2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Evidently if $k_1P_{H_2}$ is small compared to $k_2 + k_3P_{C_2H_4}$ and $k_3P_{C_2H_4} \simeq k_3$, then

$$\text{Rate} = \frac{k_1k_3P_{H_2}P_{C_2H_4}}{k_2 + k_3P_{C_2H_4}} = \frac{AP_{H_2}P_{C_2H_4}}{1 + BP_{C_2H_4}} \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

If further, at low temperatures, $k_3P_{C_2H_4} \gg k_2$

$$\text{Rate} = k_1P_{H_2} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

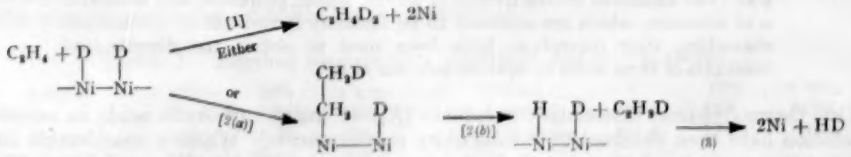
Thus the change in kinetic behaviour from dependence on the hydrogen pressure alone at low temperatures to one involving both hydrogen and ethylene at higher temperatures as shown by Toyama, zur Strassen, and in these experiments, can be interpreted on the basis that on elevation of the temperature the rate of evaporation of hydrogen $k_2\theta$ increases more rapidly than the reaction with ethylene $k_3P_{C_2H_4}\theta$, *i.e.*, the former (k_2) must have a higher energy of activation than the latter (k_3). At the temperature at which the velocity of hydrogenation undergoes an apparent inversion it is clear that $k_2 \approx k_3P_{C_2H_4}\theta$ or $k_2/k_3P_{C_2H_4} \approx 1$. Since k_2 increases more rapidly with the temperature than k_3, evidently the inversion temperature will be higher the higher the partial pressure of ethylene. Zur Strassen, working at 0·03—0·2 mm. Hg, recorded an inversion temperature of 90°. Others have found higher inversion temperatures with increase in pressure. The present experiments give 160—165° at 40 mm. Hg.

At still higher temperatures $k_2 \gg k_3P_{C_2H_4}$, and the rate of reaction will become

$$(k_1k_3/k_2)P_{H_2}P_{C_2H_4}$$

a relationship found by both zur Strassen and Toyama over their highest ranges of temperature.

It is also possible to envisage the exchange reaction between deuterium and the hydrogen in ethylene, which has long been accepted as related to the hydrogenation of ethylene, taking place in a similar manner. The following mechanism is proposed for exchange.



There are two methods of determining the rate of the exchange reaction of $C_2H_4 + D_2$, the first actually determining the deuterium content of the ethylene (Turkevich, Schissler, and Irsa, *J. Phys. Colloid Chem.*, 1951, **55**, 1078) (*i.e.*, reaction 2), and the second determining the hydrogen gas in the gas phase (Farkas, Farkas, and Rideal, *Proc. Roy. Soc.*,

1934, *A*, **146**, 630; Twigg, Thesis, and Rideal and Twigg, *Proc. Roy. Soc.*, 1939, *A*, **171**, 55) (*i.e.*, reaction 3).

The relative rates of hydrogenation and exchange (method 2) are given by $k_3 P_{C_2H_4}$ and k_2 respectively, k_2 being much smaller at low temperatures but of comparable magnitude at 165°. In experimental agreement, the temperature coefficient of the exchange reaction is much greater than that of hydrogenation, both rates being comparable at 170°.

It is also possible to correlate the results of Turkevich (*loc. cit.*) and Rideal and Twigg (*locc. cit.*). The hydrogen leaving the catalyst in the initial stages of Twigg's experiments on $C_2H_4 + D_2$ at 100—160° was almost pure hydrogen. The exchange reaction rate (reaction 2) must therefore be considerably faster than the rate of desorption of hydrogen from the surface, so that all the deuterium adsorbed has exchanged with hydrogen (contributed by the ethylene) before desorption. Thus at 170° the following picture is obtained. Deuterium is adsorbed on the catalyst on the few "active" sites. There is a rapid exchange reaction (reaction 2) which is much faster than the desorption of hydrogen or the hydrogenation reaction. Initially the deuterium on the surface is completely replaced by hydrogen. If reaction 2 is also faster than the hydrogenation at lower temperatures, then the *rapid* replacement of the deuterium on the surface by hydrogen contained in the ethylene will mean that the main product initially in hydrogenation is C_2H_6 and not $C_2H_4D_2$; *i.e.*,

$$C_2H_4(g) + D_2(g) \xrightarrow{Ni} C_2H_4(g) + 2NiD$$

$$2NiD + 2C_2H_4(g) \xrightarrow[Fast]{} 2NiH + 2C_2H_3D(g)$$

$$2NiH + C_2H_4(g) \longrightarrow C_2H_6 + 2Ni$$

This is the experimental observation of Turkevich. The suggestion has been made (Eyring, see Part I; Eley, *Quart. Rev.*, 1949, **3**, 209) that the ethane formed initially is produced by the decomposition of ethylene on the catalyst, the hydrogen adsorbed then reacting with ethylene. This cannot be true, however, because the ethane formed is far in excess of that which could be produced from the decomposition reaction on the small surface area of the nickel wire catalyst.

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The Molecular Association of Some Carboxylic Acids in Aqueous Solutions from Conductivity Data.

By D. R. CARTWRIGHT and C. B. MONK.

[Reprint Order No. 6198.]

From conductivity measurements with hydrochloric acid in aqueous dioxan and aqueous acetone, the product $\Lambda\eta/\eta_0$ (where η and η_0 are the viscosities of solvent and water) is found to be almost constant up to $\eta/\eta_0 = 1{\cdot}1$. The measured conductivities of formic, acetic, propionic, and *n*-butyric acid solutions, which are assumed to be similarly influenced by the solvent viscosities, after correction, have been used to obtain the dimerisation constants of these acids in aqueous solution at 25°.

THE thermodynamic dissociation constants (K_a) of many carboxylic acids in aqueous solution have been obtained by conductivity measurements. Where a considerable concentration range has been covered, K_a decreases with the concentration, and Katchalsky, Eisenberg, and Lifson (*J. Amer. Chem. Soc.*, 1951, **73**, 5889) considered that this can be attributed to dimerisation. Their value for the dimer dissociation constant K_d, where $K_d = [HA]^2/[H_2A_2]$, is 6·2 for acetic acid, which is in good agreement with 5·4 derived by MacDougall and Blumer (*ibid.*, 1933, **55**, 2236) from vapour pressures. However, as Davies

and Griffiths (*Z. physikal. Chem.*, Neue Folge, 1954, **2**, 353) have pointed out, MacDougall and Blumer's figure is based upon erroneous data, and a more reasonable estimate gives $K_d = 20 \pm 3$ by this method. Davies and Griffiths themselves (*loc. cit.*), from careful analyses of freezing-point and distribution measurements, obtained $K_d \sim 30$. These last two values therefore suggest that the figure of 6·2 from conductivities is too small, and a reason for this may be the neglect of the viscosities of acetic acid solutions, which increase with the acid concentration.

This point has been considered by Davies (*J. Amer. Chem. Soc.*, 1932, **54**, 3776) with reference to the evaluation of the dissociation constant K_a. MacInnes and Shedlovsky's conductivity measurements (*ibid.*, p. 1429) lead to concentration dissociation constants, and when the log values of these are plotted against c_i (where c_i is the ionic concentration), the plot should be linear with a slope value of $2 \times 0{\cdot}509$, according to Debye and Hückel's theory. Above an acid concentration of 0·01N, however, the plot curves sharply. Davies showed (*loc. cit.*) that if $\Lambda\eta/\eta_0$ is used instead of Λ, where η is the viscosity of the solution and η_0 is that of water, the plot is linear to much higher concentrations.

It is well known that correction of conductivities by the factor η/η_0 is not exactly substantiated by experiment, and to obtain some information on the error which can result in the present circumstances, the conductivity of hydrochloric acid in dioxan–water and acetone–water has been examined. Although Owen and Waters (*ibid.*, 1938, **60**, 2371) have reported measurements with the first of these solvents, they did not cover the region between water and 20% dioxan. In Table 1 we report measurements in 5% and 10%

TABLE 1. *Conductivity of hydrochloric acid in* 5% *and* 10% *dioxan at* 25°.

	5% Dioxan, $B = 160{\cdot}8$, $\Lambda^\circ = 393{\cdot}7$.					
10^4c	2·4748	3·3398	3·5131	4·2221	4·9860	6·0860
Λ	391·04	390·78	390·62	390·42	389·99	389·89
	10% Dioxan, $B = 154{\cdot}9$, $\Lambda^\circ = 366{\cdot}3$.					
10^4c	2·6665	3·2453	3·3436	4·2339	4·9112	5·0610	5·7660
Λ	363·65	362·90	362·72	362·32	361·79	361·71	361·47

mixtures. The values of Λ° were obtained by plotting $\Lambda + Bc^{\frac{1}{2}}$ against c, and extrapolating to $c = 0$; B is the theoretical Onsager slope and c is the concentration in equivs. per l.

Brownson and Cray (*J.*, 1925, **127**, 2923) have measured the conductivity of this acid in aqueous acetone. An obsolete method of deriving the cell constant was used, and a correction has been made by comparing their figures in water with those of Shedlovsky (*J. Amer. Chem. Soc.*, 1932, **54**, 1411) and multiplying the figures in aqueous acetone by the factors derived from the water figures (see Table 2).

TABLE 2. *Conductivity of hydrochloric acid in aqueous acetone at* 20°.

10^4c	4·00	10·0	20·0	40·0	100·0	200·0	Λ°	B
8% Acetone	350·8	349·3	347·7	345·4	341·9	336·9	353·5	140
16·4% Acetone	298·9	297·5	295·9	294·3	291·0	287·6	301·5	132

The products $\Lambda^\circ\eta/\eta_0$ given by the above data are shown in Table 3. They increase by about 4% for a 25% increase in viscosity with dioxan–water and decrease by the same amount for a similar increase in the viscosity of the acetone–water solvent. The nature of the organic constituent evidently has some influence.

TABLE 3. *Limiting conductivities, viscosities, and* $\Lambda^\circ\eta/\eta_0$ *values.*

Solvent	Λ°	$10^2\eta$	$\Lambda^\circ\eta/\eta_0$	Solvent	Λ°	$10^2\eta$	$\Lambda^\circ\eta/\eta_0$
Water	426·2	8·949	426·2	8% Acetone	353·5	10·6	418·7
5% Dioxan	393·7	9·76	429·4	16·4% Acetone	301·5	12·15	409·3
10% ,,	366·3	10·52	430·6				

The viscosities of dioxan–water were interpolated from Geddes's data (*ibid.*, 1933, **55**, 4832) and those of acetone–water from the International Critical Tables, **5**, 22, and from Olson and Konecny (*J. Amer. Chem. Soc.*, 1953, **75**, 5801).

In general, the figures given in Table 3 reasonably justify correcting the conductivities of carboxylic acids for the viscosities of the solutions. Following the procedure of MacInnes and Shedlovsky (*ibid.*, 1932, **54**, 1429) we can write

$$\Lambda_c = \Lambda_{(HCl)} - \Lambda_{(NaCl)} + \Lambda_{(NaA)}$$

where Λ_c is the conductivity at an ionic concentration c_i and A is the carboxylate anion. Allowing for the viscosity factor, we then have

$$\Lambda^* = \Lambda\eta/\eta_0, \ \Lambda^* c/\Lambda_c = \alpha$$

Taking K'_a as the thermodynamic dissociation constant where dimerisation is not considered, and α as the degree of dissociation, we have

$$K'_a = \alpha^2 c f_H f_A/(1 - \alpha)$$

The activity coefficients can be calculated from the limiting form of the Debye–Hückel expression, $-\log f_i = 0{\cdot}509(\alpha c)^{\frac{1}{2}}$. Extrapolation of K'_a against c gives K_a, the true thermodynamic dissociation constant. At any concentration c, if x is the true concentration of HA, then

$$x = (\alpha c)^2 f_H f_A/K_a$$

and since $[H_2A_2] = (c - \alpha c - x)/2$, the dimerisation constant K_d is given by

$$K_d = 2x^2/(c - \alpha c - x)$$

The resulting calculations are given in Table 4, the conductivity data of Saxton and Darken (*ibid.*, 1940, **62**, 846) being used for formic and *n*-butyric acids, of MacInnes and Shedlovsky for acetic acid (*loc. cit.*), and of Belcher (*ibid.*, 1938, **60**, 2744) for propionic acid. The viscosities of formic and acetic acid solutions were interpolated from data in the International Critical Tables (Vol. 5), those of propionic acid were derived from Landolt–Börnstein's "Tabellen" (Hauptband, p. 157), and those of *n*-butyric acid from the figures of Bury and Grindley (*J.*, 1936, 1003).

TABLE 4. *Dimerisation constants at 25°.*

10^3c	Λ_c	Λ^*	$10^5K'_a$	K_d	10^3c	Λ_c	Λ^*	$10^5K'_a$	K_d
Formic acid, 10^5K_a = 18·24.					Acetic acid, 10^5K_a = 1·751.				
98·86	395·04	17·917	18·21	110	50·00	386·15	7·397	1·740	15·0
185·30	393·47	13·298	18·20	152	52·30	386·10	7·242	1·743	21·1
200·14	393·24	12·817	18·19	129	100·00	385·32	5·257	1·731	16·5
207·15	393·17	12·608	18·18	121	119·45	385·09	4·822	1·732	21·7
361·80	391·55	9·6740	18·14	133	200·00	384·37	3·731	1·716	19·2
396·76	391·26	9·2611	18·10	97	230·79	384·14	3·478	1·715	21·5
463·43	390·76	8·5968	18·10	117					
546·81	390·22	7·9491	18·09	127	*n*-Butyric acid, 10^5K_a = 1·5195				
655·63	389·60	7·2882	18·04	113	14·412	378·59	12·385	1·5154	10·5
734·04	389·20	6·9082	18·02	116	26·740	378·30	10·365	1·5138	10·6
975·35	388·18	6·0295	17·91	103	30·612	377·95	8·5641	1·5120	11·9
Propionic acid, 10^5K_a = 1·347.					60·446	377·27	6·1242	1·5045	11·8
					78·623	376·98	5·3762	1·4998	11·6
75·352	381·06	5·2369	1·338	22	93·044	376·79	4·9427	1·4935	10·4
101·64	380·70	4·5175	1·335	22·5	123·53	376·44	4·2926	1·4880	11·3
192·95	379·70	3·2783	1·317	15	160·79	376·10	3·7588	1·4768	10·7
					200·32	375·81	3·3622	1·4650	10·4
					253·84	375·47	2·9805	1·4514	10·3

Discussion.—The average dimerisation constants, together with those obtained by other methods, are:

	Formic	Acetic	Propionic	*n*-Butyric
Conductivity (25°)	120 ± 12	19 ± 2	20 ± 3	11 ± 0·6
Distribution (25°)	—	28 [a]	—	10 [b]
F. p. (0°)	—	28 [a]	—	11 [b]
V. p. (25°)	—	20 ± 3 [a]	—	—

[a] Davies and Griffiths, *loc. cit.* [b] Griffiths, Thesis, University of Wales, 1952.

Considering their magnitude, the agreement by different methods is reasonable. Certainly, the present value for acetic acid is in better accord with the independent values than is that of Katchalsky *et al.* (*loc. cit.*).

It cannot be claimed that the viscosity corrections are exact, and a 5% error in these means an error of 15% in K_d. Furthermore, with formic and *n*-butyric acids, where the measurements extend to 3N and 1·2N, respectively, the higher concentrations give K_d values which decrease steadily from those given in Table 4. This may be because errors in the viscosity factor become more important in these regions, or it may be that K_a, the thermodynamic dissociation constant, is different from what it is in dilute solutions. Since the dielectric constants of these solutions have not yet been measured, an estimate of possible changes in K_a cannot be made.

Apart from propionic acid, our K_a values are slightly different from those given by the original authors. The reason for this is that their method was to plot the logarithm of the concentration dissociation constants against $\sqrt{c_i}$ and extrapolate. In the present analysis, K_a' is practically constant in very dilute solutions and a more exact extrapolation is possible. A final adjustment was made by trying slight variation in the extrapolated value of K_a until K_d showed no sudden trends with the acid concentration.

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Hydroxylation of Flavanones in the 3-Position.

By V. B. MAHESH and T. R. SESHADRI.

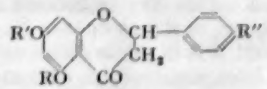
[Reprint Order No. 6233.]

Oxidation of acetoxyflavanones with Fenton's reagent in acid medium yields 3-hydroxy-compounds with simultaneous deacetylation in the 5-position. As by-products arise binuclear compounds by dehydrogenative coupling in the 3-position. The method is of interest in biogenesis.

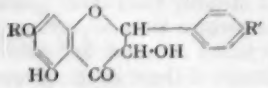
VARIOUS flavanones are found in Nature along with their 3-hydroxy-derivatives (flavanolones) (Pew, *J. Amer. Chem. Soc.*, **1948**, **70**, 3031; Lindstedt, *Acta Chem. Scand.*, **1951**, **5**, 121; Mahesh and Seshadri, *J. Sci. Ind. Res., India*, 1954, **13**, *B*, 835). This suggests the existence of a phytochemical hydroxylation process affecting the 3-position of flavanones. Hydroxylation of flavanones at position 3 has been achieved in the laboratory by bromination (Zemplen and Bognar, *Ber.*, **1943**, **76**, 452), iodination (Goel, Narasimhachari, and Seshadri, *Proc. Indian Acad. Sci.*, **1954**, **39**, *A*, 254), and lead tetra-acetate (Oyamada, *J. Chem. Soc. Japan*, 1943, **64**, 331, **471**; Cavill, Dean, McGookin, Marshall, and Robertson, *J.*, 1954, 4573; Kotake, Sakan, and Kubota, *Chem. and Ind.*, 1954, 1562). The use of Fenton's reagent in acid medium has now been examined. This free-radical reaction proceeds satisfactorily and provides good support for the biogenesis of flavanolones because according to Haber and Willstätter (*Ber.*, 1931, **64**, 2844) enzyme oxidation involves free radicals and, further, Fenton's method and enzymic oxidation of a large variety of organic compounds yield similar products (Mackinnon and Waters, *J.*, 1953, 323).

When naringenin triacetate (I; R = R′ = Ac, R″ = OAc) was oxidised by Fenton's reagent in acid medium, a mixture of two compounds was obtained. One of these formed a crystalline lead salt from which it could be recovered. Its ferric chloride colour, composition, and properties suggested that it was 7 : 4′-diacetoxy-3 : 5-dihydroxyflavanone (II; R = Ac, R′ = OAc). That deacetylation had taken place in the 5-position was supported by the observation that naringenin triacetate (I; R = R′ = Ac, R″ = OAc) undergoes partial deacetylation in sulphuric acid, yielding the 7 : 4′-diacetate. The formation of the lead salt depends on the presence of 3- and 5-hydroxyl groups since, among known compounds, naringenin diacetate (I; R = H, R′ = Ac, R″ = OAc) and pinostrobin (I; R = R″ = H, R′ = Me) do not form basic lead salts whereas pinobanksin (II; R =

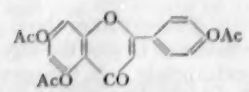
R′ = H) and its 7-methyl ether (II; R = Me, R′ = H) do. The constitution of the oxidation product as (II; R = Ac, R′ = OAc) is confirmed by its formation also by the oxidation of naringenin diacetate (I; R = H, R′ = Ac, R″ = OAc) under the same conditions. Further, acid hydrolysis yielded 3-hydroxynaringenin (II; R = H, R′ = OH) (Goel, Narasimhachari, and Seshadri, *loc. cit.*). It was dehydrated by acetic anhydride to apigenin triacetate (III).



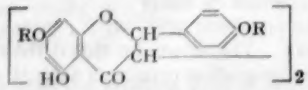
(I)



(II)



(III)



(IV)

The second product of Fenton oxidation yielded on deacetylation with acid a compound which agreed in composition and molecular weight with the diflavanone formula (IV; R = H). The parent compound should therefore be the partial acetate (IV; R = Ac) and its properties and composition were in agreement with this. Fenton's oxidation of a number of other organic compounds is known to produce such bimolecular products (Merz and Waters, *J.*, 1949, 2427).

Similar oxidation of 5 : 7-diacetoxyflavanone (I; R = R′ = Ac, R″ = H) gave 7-acetoxy-3 : 5-dihydroxyflavanone (II; R = Ac, R′ = H) which was hydrolysed to 3 : 5 : 7-trihydroxyflavanone (II; R = R′ = H).

Earlier, potassium permanganate had been used for the hydroxylation of other compounds in the position α to a carbonyl group : 7 : 2′ : 4′-trimethoxy*iso*flavanone yielded its 3-hydroxy-derivative (Robertson and Whalley, *J.*, 1954, 1440), and 2-benzyl-4 : 6-dimethoxycoumaranone its 2-hydroxy-derivative (Gripenberg, *Acta Chem. Scand.*, 1953, **7**, 1323). This reagent has now been employed for the conversion of 5 : 7-diacetoxyflavanone (I; R = R′ = Ac, R″ = H) into 7-acetoxy-3 : 5-dihydroxyflavanone (II; R = Ac, R′ = H), but it gives rather poor yields compared with Fenton's reagent whose use appears therefore to be of preparative value.

Experimental

Hydroxylation of Naringenin Triacetate (I; R = R′ = Ac, R″ = OAc) *to* 7 : 4′-*Diacetoxy*-3 : 5-*dihydroxyflavanone* (II; R = Ac, R′ = OAc).—To a stirred suspension of finely powdered naringenin triacetate (1 g.) in 2N-sulphuric acid (100 c.c.) at 0° hydrogen peroxide (5-vol.; 50 c.c.) and ferrous sulphate solution (2%; 50 c.c.) were run in simultaneously during 45 min. The mixture was then extracted repeatedly with ether, and the extract evaporated, yielding a yellow solid. This was dissolved in alcohol (50 c.c.), and a saturated alcoholic solution of basic lead acetate (150 c.c.) added. A crystalline yellow lead salt separated (600 mg.) which was filtered off (filtrate F) and decomposed with hydrogen sulphide in alcohol. The *product* obtained by evaporating the alcoholic solution crystallised from aqueous alcohol as colourless needles and small rectangular prisms (0·25 g.), m. p. 136—137° (Found : C, 61·0; H, 4·5. $C_{19}H_{16}O_8$ requires C, 61·3; H, 4·3%). It gave a brownish-red colour with ferric chloride and a red colour with magnesium or zinc and hydrochloric acid.

The mother-liquor (F) was heated to the b. p. and hydrogen sulphide passed into it. Lead sulphide was filtered off and the filtrate evaporated to dryness. The residual *di*-(7 : 4′-*diacetoxy*-5-*hydroxyflavanon*-3-*yl*) crystallised from alcohol as colourless flat needles and rectangular plates, m. p. 192—194° (Found : C, 63·9; H, 4·7. $C_{38}H_{30}O_{14}$ requires C, 64·2; H, 4·2%). Yield 250 mg. It gave a brownish-red colour with ferric chloride, a red colour with magnesium and hydrochloric acid, and a pink colour with zinc and hydrochloric acid. This partial acetate (150 mg.) was hydrolysed for 15 min. with boiling alcoholic hydrochloric acid (50 c.c.; 1 : 1). Addition of water (50 c.c.) yielded a sticky solid which crystallised from ethyl acetate–light petroleum as colourless rectangular tablets and prisms, m. p. 210—212° [Found : C, 65·9; H, 4·0%; *M* (cryoscopic), 539. $C_{30}H_{22}O_{10}$ requires C, 66·4; H, 4·0%; *M*, 542]. It gave a reddish-violet colour with ferric chloride, a red colour with magnesium and hydrochloric acid,

and a faint pink colour with zinc and hydrochloric acid. Attempts to dehydrogenate it with selenium dioxide in acetic anhydride led to decomposition.

Hydroxylation of Naringenin Diacetate (I; R = H, R′ = Ac, R″ = OAc) *to* 7 : 4′-*Diacetoxy*-3 : 5-*dihydroxyflavanone* (II; R = Ac, R′ = OAc).—Naringenin diacetate (0·5 g.), prepared by the partial acetylation of naringenin, was subjected to Fenton oxidation and the product worked up as in the above experiment. A pale yellow substance (60 mg.) obtained by the decomposition of the lead salt had m. p. 136—137° alone or mixed with the product obtained by hydroxylation of naringenin triacetate; the mixed m. p. with naringenin diacetate (m. p. 140—141°) was depressed. Naringenin diacetate did not form a basic lead salt. A second product (m. p. 192—194°) which did not give a lead salt was identical with the similar one obtained in the oxidation of naringenin triacetate.

3-*Hydroxynaringenin* (II; R = H, R′ = OH).—The diacetoxyflavanone, m. p. 136—137°, was hydrolysed with alcoholic hydrochloric acid to 3-hydroxynaringenin, flesh-coloured rhombohedral prisms, m. p. 238—240° (decomp.) (from aqueous alcohol), giving a violet colour with ferric chloride and a red colour with magnesium or zinc and hydrochloric acid. A mixed m. p. with Goel, Narasimhachari and Seshadri's sample (*loc. cit.*) was undepressed.

Dehydration of 3-*Hydroxynaringenin to Apigenin Triacetate* (III).—3-Hydroxynaringenin (0·25 g.), refluxed with acetic anhydride (2 c.c.) for 2 hr., afforded apigenin triacetate, rectangular plates (0·1 g.), m. p. 180—181° (from ethyl acetate–light petroleum).

Hydroxylation of 5 : 7-*Diacetoxyflavanone* (I; R = R′ = Ac, R″ = H) *to* 7-*Acetoxy*-3 : 5-*dihydroxyflavanone* (II; R = Ac, R′ = H).—(a) *Fenton's reagent.* 5 : 7-Diacetoxyflavanone (1 g.) was subjected to Fenton oxidation as in the case of naringenin triacetate. The basic lead salt yielded on decomposition a *product* which crystallised from aqueous alcohol as needles, m. p. 90—92° (0·1 g.) (Found: C, 64·5; H, 4·9. $C_{17}H_{14}O_6$ requires C, 65·0; H, 4·5%). It gave a brownish-red colour with ferric chloride, a red colour with magnesium and hydrochloric acid, and a pink colour with zinc and hydrochloric acid.

(b) *Neutral permanganate.* 5 : 7-Diacetoxyflavanone (1 g.) was dissolved in acetone (100 c.c.), finely powdered permanganate (5 g.) added, and the mixture stirred for 4 hr. at room temperature. Water (500 c.c.) was then added and the manganese dioxide dissolved by use of sulphur dioxide. The solution was extracted with ether (3 × 200 c.c.), and the ether extract was washed with aqueous sodium hydrogen carbonate and evaporated. The residue was converted by way of the lead salt into the preceding product, needles (35 mg.), m. p. and mixed m. p. 90—92°.

3 : 5 : 7-*Trihydroxyflavanone* (II; R = R′ = H).—7-Acetoxy-3 : 5-dihydroxyflavanone was deacetylated by alcoholic hydrochloric acid to 3 : 5 : 7-trihydroxyflavanone, rectangular prisms (from aqueous alcohol), m. p. and mixed m. p. 172—173° (50 mg.).

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Carbohydrate Phosphates. Part I. Synthesis of Derivatives of Some aldehydo-*Sugar Phosphates.*

By J. L. BARCLAY, A. B. FOSTER, and W. G. OVEREND.

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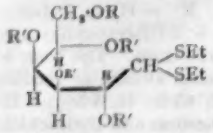
The synthesis is described of some phosphorylated derivatives of *aldehydo*-D-galactose and its 2-deoxy-analogue and of *aldehydo*-2-deoxy-D-glucose. The action of hydrogen bromide in acetic acid on 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (XIII) and 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-glucose diethyl mercaptal (XVII) did not give the expected replacement of the triphenylmethyloxy-group by bromine; instead, a simultaneous fission occurred, which resulted, in the case of (XIII), in the formation of ethyl triphenylmethyl sulphide.

THERE are two main approaches which can be made to the synthesis of simple nucleotides. One involves the *initial* formation of glycosylamine (*i.e.*, nucleoside synthesis) and subsequent phosphorylation of the carbohydrate moiety, a method which has been extensively and successfully used by Todd and his colleagues (*e.g.*, *J.*, 1946, 647). For several reasons

it may prove more difficult to use this reaction sequence to synthesise deoxy-sugar nucleotides [Foster, *Farmakoterapi* (Oslo), **1951**, No. 3, 1], especially those of the purine type. The alternative route, which has not been investigated, requires the formation of a phosphorylated *aldehydo*-sugar and condensation of this with a base to form finally the glycosylamine grouping. As a contribution to the latter approach we describe in this paper the synthesis of some phosphorylated *aldehydo*-sugars. Observations on the condensation reaction will form the subject of a separate communication.

Various intermediates may be utilised for the synthesis of *aldehydo*-sugar phosphates, *e.g.*, mercaptals (Wolfrom, *J. Amer. Chem. Soc.*, **1929**, **51**, 2188), semicarbazones (Major and Cook, *J. Amer. Chem. Soc.*, **1936**, **58**, 2474), or thiol esters (Wolfrom and Karabinos, *J. Amer. Chem. Soc.*, **1946**, **68**, 724) and glyconic amides (Haworth, Peat, and Whetstone, *J.*, 1938, 1975), and certain cyclic acetals of some polyalcohols (Bourne, Corbett, and Stacey, *J.*, **1952**, 2810; Foster and Overend, *J.*, **1951**, 680). In this work sugar diethyl mercaptals have been used as intermediates.

Reaction of D-galactose diethyl mercaptal (I) with carefully purified triphenylmethyl chloride (1 mol.) in pyridine and then with acetic anhydride in the same solvent gives 2 : 3 : 4 : 5-tetra-*O*-acetyl-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (II) in good



	R	R'
(I)	H	H
(II)	CPh_3	Ac
(III)	H	Ac
(IV)	$(PhO)_2PO$	Ac

	R	R'
(V)	CPh_3	Bz
(VI)	H	Bz
(VII)	$(PhO)_2PO$	Bz
(VIII)	Ac	Ac

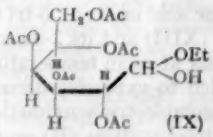
yield. Elimination of the triphenylmethyl group from (II) as triphenylmethyl bromide is achieved by careful treatment at 0° with acetic acid containing the theoretical amount of hydrogen bromide (cf. Wolfrom, Quinn, and Christman, *J. Amer. Chem. Soc.*, **1935**, **57**, 713), and 2 : 3 : 4 : 5-tetra-*O*-acetyl-D-galactose diethyl mercaptal (III) is obtained. The possibility of hydrolysis and catalyst poisoning precludes the use of either aqueous acid (Kuhn, Rudy, and Weygand, *Ber.*, **1936**, **69**, 1543) or hydrogenation (Micheel, *Ber.*, 1932, **65**, 262) to effect this conversion. In similar manner D-galactose diethyl mercaptal (I) was converted *via* (V) into 2 : 3 : 4 : 5-tetra-*O*-benzoyl-D-galactose diethyl mercaptal (VI).

Phosphorylation of 2 : 3 : 4 : 5-tetra-*O*-acetyl-D-galactose diethyl mercaptal (III) with diphenyl phosphorochloridate in pyridine proceeded readily at 0°, to yield crystalline 2 : 3 : 4 : 5-tetra-*O*-acetyl-D-galactose diethyl mercaptal 6-(diphenyl phosphate) (IV) in 93% yield. Under comparable conditions phosphorylation of 2 : 3 : 4 : 5-tetra-*O*-benzoyl-D-galactose diethyl mercaptal (VI) does not proceed and prolonged reaction (48 hours at 35°, followed by 0·5 hour at 60°) is necessary to give the difficultly crystalline phosphate (VII) in moderate yield (56%). This derivative was not studied further.

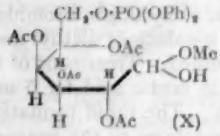
A general procedure for fission of thio-groups has been reported by Wolfrom (*J. Amer. Chem. Soc.*, 1930, **52**, 2464), involving the use of mercuric chloride in the presence of cadmium carbonate. A detailed study of the reaction led to the conditions described in the Experimental section. In model experiments 2 : 3 : 4 : 5 : 6-penta-*O*-acetyl-D-galactose diethyl mercaptal (VIII) gave 2 : 3 : 4 : 5 : 6-penta-*O*-acetyl-*aldehydo*-D-galactose. This crystallised with a molecule of ethanol which could be removed only with difficulty, by repeated crystallisation from dry toluene, and the ethanol may be present in a hemiacetal linkage as in (IX) (cf. Wolfrom, *loc. cit.*). This point, together with other related observations will be discussed in a future publication. A crystalline semicarbazone was easily prepared from 2 : 3 : 4 : 5 : 6-penta-*O*-acetyl-*aldehydo*-D-galactose monoethanolate.

Under the same conditions, 2 : 3 : 4 : 5-tetra-*O*-acetyl-D-galactose diethyl mercaptal 6-(diphenyl phosphate) (IV) afforded 2 : 3 : 4 : 5-tetra-*O*-acetyl-*aldehydo*-D-galactose 6-(diphenyl phosphate) monomethanolate [represented as a hemiacetal (X)] (after crystallisation from methanol), from which a crystalline semicarbazone (XI) was prepared. It is clear that with the reaction sequence adopted, crystalline phosphorylated *aldehydo*-sugar derivatives can be obtained and that the aldehydo-group behaves normally with a usual reagent employed for characterisation.

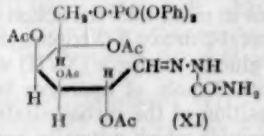
Although extension of the reaction sequence I → II → III → IV → X to the 2-deoxy-sugar series gave the desired products, from our viewpoint it was not completely successful since we did not obtain all the intermediates in crystalline form.



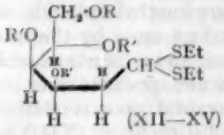
(IX)



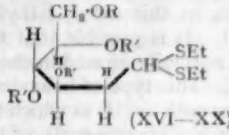
(X)



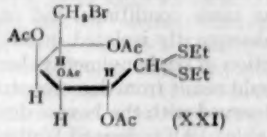
(XI)



(XII—XV)



(XVI—XX)



(XXI)

	R	R′
(XII)	CPh_3	H
(XIII)	CPh_3	Ac
(XIV)	H	Ac
(XV)	$(PhO)_2PO$	Ac
(XVI)	H	H

	R	R′
(XVII)	CPh_3	Ac
(XVIII)	H	Ac
(XIX)	Ac	Ac
(XX)	$(PhO)_2PO$	Ac

2-Deoxy-D-galactose diethyl mercaptal was converted successively into crystalline 2-deoxy-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (XII) and thence into crystalline 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (XIII). Cleavage of the triphenylmethyl group from (XIII) occurred on careful treatment at 0° with hydrogen bromide (1 mol.) in dry acetic acid but the product was syrupy. Elemental analysis agreed with that for 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-D-galactose diethyl mercaptal (XIV) but crystalline derivatives could not be obtained. The syrupy methanesulphonyl derivative of (XIV) readily underwent an exchange reaction with sodium iodide in dry acetone, providing some indication that the methanesulphonyloxy-residue was located at position 6, and that cleavage of the triphenylmethyl group from (XIII) was not accompanied by concomitant acetyl migration.

In like manner 2-deoxy-D-glucose diethyl mercaptal (XVI) was converted *via* (XVII) into 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-D-glucose diethyl mercaptal (XVIII) which was obtained crystalline only with difficulty. On acetylation this gave authentic 3 : 4 : 5 : 6-tetra-*O*-acetyl-2-deoxy-D-glucose diethyl mercaptal (XIX).

Reaction of the tri-acetates (XIV) or (XVIII) with diphenyl phosphorochloridate in pyridine gave syrupy diphenyl phosphates, probably (XV) and (XX) respectively, and removal of the ethylthio-groups then yielded syrupy products which were sulphur-free but could not be characterised as crystalline derivatives.

It is worthy of comment that reaction of 2 : 3 : 4 : 5-tetra-*O*-acetyl-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (II) with hydrogen bromide in acetic acid may proceed in two stages (cf. Wolfrom, Quinn, and Christman, *loc. cit.*). As mentioned, treatment with 1·0 mol. (or preferably slightly less than 1·0 mol.) of hydrogen bromide in dry acetic acid at 0° for a very few minutes led to cleavage of the triphenylmethyl group to give 2 : 3 : 4 : 5-tetra-*O*-acetyl-D-galactose diethyl mercaptal (III). The use of more hydrogen bromide gave 2 : 3 : 4 : 5-tetra-*O*-acetyl-6-bromo-6-deoxy-D-galactose diethyl mercaptal (XXI). Presumably the two reactions are consecutive.

Replacement of the acetate groups by benzoate groups, as in 2 : 3 : 4 : 5-tetra-*O*-benzoyl-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal, confers considerable stability on the molecule since treatment with excess of hydrogen bromide in acetic acid gave a good yield (67%) of 2 : 3 : 4 : 5-tetra-*O*-benzoyl-D-galactose diethyl mercaptal with insignificant formation of the 6-bromo-6-deoxy-derivative. This may be due to a shielding effect by the benzoate groups. In this connection it is interesting that attempts to triphenylmethylate the alcohols (XIV) or (XVIII) were unsuccessful and it is possible that the

converse effect of the presence of the acetate groups might sterically hinder the approach of the large chlorotriphenylmethane molecule.

Alkyl bromides such as (XXI) have some value as intermediates in phosphate and polyphosphate synthesis (cf. *e.g.*, Clark, Todd, and Zussman, *J.*, 1951, 2952) and it was with this in mind that the action of excess of hydrogen bromide in acetic acid on 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (XIII) and its 2-deoxy-D-glucose analogue (XVII) was examined. Treatment of the former at room temperature with 2 mols. of hydrogen bromide in acetic acid for 5 minutes led to extensive decomposition of the carbohydrate moiety. The rapid formation of insoluble triphenylmethyl bromide which normally occurs in reactions of the hexose derivatives such as (II) under the same conditions, did not occur in this case. Ethyl triphenylmethyl sulphide was subsequently isolated in 68% yield. It is possible that this product arose by the interaction of triphenylmethyl bromide, normally formed in the reaction, and ethanethiol which could result from demercaptolation. This type of behaviour does not appear to have been observed with the hexose derivatives such as (II) in which the mercaptal group is relatively stable. An increased lability towards acidic reagents, of the 1-substituents in (XIII) and (XVII), is to be expected because of the presence of the 2-methylene group (see Butler, Laland, Overend, and Stacey, *J.*, 1950, 1433, and papers in the same series).

The action of excess of hydrogen bromide on 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-glucose diethyl mercaptal (XVII) did not yield ethyl triphenylmethyl sulphide but an unidentified product. Thus the action of hydrogen bromide in acetic acid on the 2-deoxy-hexose derivatives (XIII) and (XVII) is more complex than in the case of the hexose analogue (II) and does not give rise to the expected halogeno-derivatives.

Experimental

[α] refers to solutions in $CHCl_3$ unless otherwise stated.

Fission of 2 : 3 : 4 : 5 : 6-*Penta*-O-*acetyl*-D-*galactose Diethyl Mercaptal* (VIII).—A solution of the mercaptal (20 g.) in aqueous acetone was treated with mercuric chloride (3·6 mol.) and excess of cadmium carbonate as described by Wolfrom (*loc. cit.*). The charcoal treatment of the reaction mixture recommended by this author was omitted since it considerably reduced the yield. 2 : 3 : 4 : 5 : 6-Penta-*O*-acetyl-*aldehydo*-D-galactose monoethanolate (IX) (13·2 g., 75%) was isolated, with m. p. 126—128°. From (IX), 2 : 3 : 4 : 5 : 6-penta-*O*-acetyl-*aldehydo*-D-galactose (m. p. 118°) and its semicarbazone (m. p. 200°) were obtained as described by Wolfrom (*loc. cit.*).

2 : 3 : 4 : 5-*Tetra*-*O*-*acetyl*-D-*galactose Diethyl Mercaptal* 6-(*Diphenyl Phosphate*) (IV).—A solution of 2 : 3 : 4 : 5-tetra-*O*-acetyl-D-galactose diethyl mercaptal (3 g., 1 mol.), prepared from 2 : 3 : 4 : 5-tetra-*O*-acetyl-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal by the method of Wolfrom, Quinn, and Christman (*loc. cit.*), in dry pyridine (12 ml.) was treated with diphenyl phosphorochloridate (2 g., 1·1 mol.) at 0° for 12 hr. Pouring the mixture into ice water (200 ml.) gave a syrup which soon solidified. Recrystallisation from methanol afforded the *phosphate* as needles (4·2 g., 93%), m. p. 82°, $[\alpha]_D^{18}$ −6° (*c*, 2·0) (Found: C, 52·5; H, 5·7; S, 9·1; P, 4·7. $C_{30}H_{39}O_{12}S_2P$ requires C, 52·5; H, 5·7; S, 9·3; P, 4·5%).

2 : 3 : 4 : 5-*Tetra*-*O*-*acetyl*-aldehydo-D-*galactose* 6-(*Diphenyl Phosphate*) (X).—The preceding mercaptal (IV) (11·6 g.) was dissolved in acetone (50 ml.) and water (17 ml.) in which was suspended finely powdered cadmium carbonate (17 g.). The mixture was stirred vigorously and a solution of mercuric chloride (15 g.) in acetone (45 ml.) was added gradually during 1 hr. The mixture was stirred vigorously for a further 20 hr. with frequent additions of fresh cadmium carbonate, then filtered, the residue was washed with acetone, and the combined filtrate and washings were evaporated under reduced pressure at 35°. Final traces of water were removed by storage *in vacuo* over phosphoric oxide. The solid residue was extracted with warm chloroform (4 × 50 ml.), and the combined extracts were washed successively with water, aqueous potassium iodide (10%), and water, and then dried ($MgSO_4$). Concentration of the chloroform solution gave a pale yellow syrup which crystallised from methanol. Recrystallisation from acetone–ether–light petroleum (b. p. 60—80°) gave the *phosphate* (5·1 g., 49%) as needles, m. p. 97°, $[\alpha]_D^{18}$ +24° (*c*, 2·0) (Found: C, 52·95; H, 5·3; P, 5·05. $C_{26}H_{29}O_{13}P,CH_3{\cdot}OH$ requires C, 52·9; H, 5·4; P, 5·1%). It slowly restored the colour to Schiff's reagent.

Treatment of this product (0·1 g.) in 60% aqueous ethanol (3 ml.) containing sodium acetate

(0·02 g.) with semicarbazide hydrochloride (0·03 g.) at 0° for 12 hr. gave the *semicarbazone* (40 mg., 39%), m. p. 152° (from methanol) (Found: C, 50·4; H, 5·3; N, 6·5; P, 4·9. $C_{27}H_{32}O_{13}N_3P$ requires C, 50·9; H, 5·0; N, 6·6; P, 4·9%).

2 : 3 : 4 : 5-*Tetra*-O-*benzoyl*-D-*galactose Diethyl Mercaptal* (VI).—Treatment of 2 : 3 : 4 : 5-tetra-*O*-benzoyl-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (m. p. 141°, $[\alpha]_D^{20}$ −24°) by essentially the method of Wolfrom *et al.* (*loc. cit.*) gave 2 : 3 : 4 : 5-tetra-*O*-benzoyl-D-galactose diethyl mercaptal (67%), m. p. 96°, $[\alpha]_D^{20}$ −6·0° (*c*, 2·0). Wolfrom *et al.* record m. p. 96—97°, $[\alpha]_D^{20}$ −6·8°.

2 : 3 : 4 : 5-*Tetra*-O-*benzoyl*-D-*galactose Diethyl Mercaptal* 6-(*Diphenyl Phosphate*) (VII).—A solution of 2 : 3 : 4 : 5-tetra-*O*-benzoyl-D-galactose diethyl mercaptal (2 g., 1 mol.) in dry pyridine (10 ml.) was treated with diphenyl phosphorochloridate (1 g., 1·25 mol.) for 48 hr. at 35° and then at 60° for 30 min., then poured into ice–water (100 ml.), and the resultant solution extracted with chloroform (4 × 25 ml.). The combined extracts were washed successively with aqueous potassium hydrogen sulphate, water, aqueous potassium hydrogen carbonate, and water, and then dried ($MgSO_4$). Evaporation under diminished pressure yielded a syrup which separated from ethanol as an amorphous solid. Recrystallisation from ethanol–*n*-pentyl alcohol gave the *product* (1·6 g., 56%), m. p. 60—62°, $[\alpha]_D^{17}$ −4° (*c*, 2·0) (Found: C, 64·2; H, 5·15; S, 6·7; P, 3·5. $C_{50}H_{47}O_{12}S_2P$ requires C, 64·2; H, 5·0; S, 6·8; P, 3·3%).

2-*Deoxy*-D-*galactose Diethyl Mercaptal*.—Prepared according to the method of Overend, Shafizadeh, and Stacey (*J.*, 1950, 671) the compound had m. p. 106—107°, $[\alpha]_D^{18}$ +45° (*c*, 0·8 in EtOH). Overend *et al.* give m. p. 107—108°, $[\alpha]_D^{20}$ +40° in MeOH.

2-*Deoxy*-6-O-*triphenylmethyl*-D-*galactose Diethyl Mercaptal* (XII).—A solution of 2-deoxy-D-galactose diethyl mercaptal (1·0 g.) in dry pyridine (8 ml.) was treated with triphenylmethyl chloride (1·03 g.) for 30 hr. at room temperature, then diluted with ice-water (100 ml.), and the syrup which separated was washed with water by decantation. The *mercaptal* (0·87 g., 46%), crystallised from methanol, had m. p. 92°, $[\alpha]_D^{17}$ +24·8° (*c*, 1·29) (Found: C, 67·6; H, 7·0; S, 12·6. $C_{29}H_{36}O_4S_2$ requires, C, 68·0; H, 7·0; S, 12·5%).

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-6-O-*triphenylmethyl*-D-*galactose Diethyl Mercaptal* (XIII).—A solution of 2-deoxy-D-galactose diethyl mercaptal (19 g.) in dry pyridine (*ca.* 80 ml.) was treated with triphenylmethyl chloride (19·6 g.) for 30 hr. at 35°. Acetic anhydride (106 ml.) was then added slowly to the cooled solution, with stirring during 1 hr. The mixture was set aside at 35° for a further 30 hr. and then poured into ice–water (3 l.) containing acetic acid (50 ml.). The syrup which separated solidified during 12 hr. and the product was then collected and washed with water. Recrystallisation from methanol afforded needles of the *product* (30 g., 66%), m. p. 91°, $[\alpha]_D^{18}$ −10·7° (*c*, 3·0) (Found: C, 65·8; H, 6·8; S, 9·8. $C_{35}H_{42}O_7S_2$ requires C, 65·8; H, 6·6; S, 10·0%).

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-D-*galactose Diethyl Mercaptal* (XIV).—To a chilled solution of 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-galactose diethyl mercaptal (10 g. in the minimum amount of glacial acetic acid) a 10% solution of hydrogen bromide in glacial acetic acid (0·95 mol.) was added accurately from a microburette. The resultant mixture was filtered after 1 min. and the filtrate immediately poured on a mixture of ice and sodium hydrogen carbonate. Water was then added and the solution extracted with chloroform (6 × 25 ml.). The combined extracts were washed successively with water, aqueous sodium hydrogen carbonate, and water and dried ($CaCl_2$). Evaporation of the solution under diminished pressure at 35° (bath) gave a syrup which partly crystallised on treatment with methanol and water. The crystals (0·2 g.) had m. p. 90—91° alone and in admixture with starting material. Concentration of the mother-liquors and distillation of the residue afforded 3 : 4 : 5-*tri*-O-*acetyl*-2-*deoxy*-D-*galactose diethyl mercaptal* (4·9 g., 79%) as a pale yellow syrup, b. p. 200—205° (bath)/0·1 mm., n^{18} 1·5004, $[\alpha]_D^{20}$ +23·3° (*c*, 3·18) (Found: C, 48·7; H, 7·2; S, 16·4. $C_{16}H_{28}O_7S_2$ requires C, 48·4; H, 7·1; S, 16·2%).

Attempts to prepare a crystalline benzoate, 3 : 5-dinitrobenzoate, carbanilate, triphenylmethyl ether, toluene-*p*-sulphonate, or methanesulphonate were unsuccessful. Oxidation with perphthalic acid did not afford a crystalline derivative.

Action of Excess of Hydrogen Bromide on 3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-6-O-*triphenylmethyl*-D-*galactose Diethyl Mercaptal* (XIII).—An ice-cold solution of the mercaptal (2·5 g.) in glacial acetic acid (15 ml.) was treated with a 20% solution of hydrogen bromide in glacial acetic acid (2 mol.) for 5 min. at room temperature. The mixture was then filtered and the filtrate poured on a mixture of ice and sodium hydrogen carbonate. After dilution with water the solution was extracted with chloroform (4 × 15 ml.), and the combined extracts were washed with aqueous sodium hydrogen carbonate and water and dried ($CaCl_2$). Evaporation left a syrup which

crystallised on trituration with methanol. Recrystallisation from methanol gave colourless needles (0·9 g.) of ethyl triphenylmethyl sulphide, m. p. 127° (Found: C, 82·8; H, 6·3; S, 10·5. Calc. for $C_{21}H_{20}S$: C, 82·9; H, 6·6; S, 10·5%). Meyer and Fischer (*J. prakt. Chem.*, 1910, **82**, 525) cite m. p. 126°.

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-D-*galactose Diethyl Mercaptal* 6-(*Diphenyl Phosphate*) (XV).—Diphenyl phosphorochloridate (6·8 g.) was added to a chilled solution of **3 : 4 : 5**-tri-*O*-acetyl-2-deoxy-D-galactose diethyl mercaptal (10 g.) in dry pyridine (40 ml.), and the mixture set aside at 0° overnight and then poured into ice–water (300 ml.). The aqueous solution was extracted with chloroform (4 × 50 ml.), and the combined extracts were washed, dried, and evaporated under diminished pressure. The residual syrup was dried at 30° for 4 hr. *in vacuo* to give the *product* (12·6 g., 79%) as a pale yellow syrup, n^{18} 1·5196, $[\alpha]_D^{18}$ +12° (*c*, 2·0) (Found: C, 52·4; H, 6·2; S, 10·4. $C_{28}H_{37}O_{10}S_2P$ requires C, 53·5; H, 5·9; S, 10·2%).

Attempted removal of the ethylthio-groups as previously described gave a product which contained phosphorus but not sulphur, but it was not crystalline. It restored the colour to Schiff's reagent.

2-*Deoxy*-D-*glucose Diethyl Mercaptal* (XVI).—Prepared according to the method of Hughes, Overend, and Stacey (*J.*, 1949, 2846) this compound had m. p. 134°, $[\alpha]_D^{19}$ +10° (*c*, 1·0 in EtOH).

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-6-O-*triphenylmethyl*-D-*glucose Diethyl Mercaptal* (XVII).—A solution of 2-deoxy-D-glucose diethyl mercaptal (10 g.) in dry pyridine (63 ml.) was treated with triphenylmethyl chloride (10·4 g.) for 30 hr. at 35°, then cooled to 0°, and acetic anhydride (56 ml.) was slowly added during 30 min. After a further 30 hr. at 35° the mixture was diluted with ice–water (2 l.) containing glacial acetic acid (30 ml.). The syrup which separated had crystallised after 4 hr. It was collected, washed with water, and recrystallised from aqueous methanol. The *product* (18·7 g., 78%) was obtained as stout needles, m. p. 104°, $[\alpha]_D^{18}$ +43·3° (*c*, 3·0) (Found: C, 65·7; H, 6·3; S, 9·8. $C_{38}H_{42}O_7S_2$ requires C, 65·8; H, 6·6; S, 10·0%).

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-D-*glucose Diethyl Mercaptal* (XVIII).—To a chilled solution of 3 : 4 : 5-tri-*O*-acetyl-2-deoxy-6-*O*-triphenylmethyl-D-glucose diethyl mercaptal (10 g.) in glacial acetic acid a 10% solution of hydrogen bromide in glacial acetic acid (0·95 mol.) was added accurately. After 1 min. the precipitated triphenylmethyl bromide was removed and the filtrate poured on ice and sodium hydrogen carbonate. The mixture was worked up as described in the preparation of (XIV). The syrup obtained was dissolved in aqueous methanol, from which unchanged starting material (0·63 g.) separated. Concentration of the mother-liquors gave a syrup which was distilled, to give a pale yellow viscous syrup (4·3 g., 62%), b. p. 190—200° (bath-temperature)/0·01 mm., n^{17} 1·5159. The distillate partly crystallised on trituration with methanol and on recrystallisation from aqueous methanol the *product* (0·63 g.) was obtained as hexagonal prisms, m. p. 73°, $[\alpha]_D^{21}$ +38·7° (*c*, 3·0) (Found: C, 48·1; H, 6·9; S, 15·8. $C_{16}H_{26}O_7S_2$ requires C, 48·4; H, 7·1; S, 16·2%).

The crystalline material was very soluble in methanol and was difficult to free completely from adhering syrup: in subsequent reactions the syrup was used directly.

Acetylation of the syrup (0·6 g.) with pyridine (5 ml.) and acetic anhydride (3 ml.) by the usual method gave **3 : 4 : 5 : 6**-tetra-*O*-acetyl-2-deoxy-D-glucose diethyl mercaptal (0·48 g.), m. p. and mixed m. p. 76°, $[\alpha]_D^{18}$ +35° (*c*, 2·0 in MeOH) (Found: C, 49·3; H, 6·7; S, 14·9. Calc. for $C_{18}H_{30}O_8S_2$: C, 49·3; H, 6·8; S, 14·6%).

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-6-O-*methanesulphonyl*-D-*glucose Diethyl Mercaptal*.—Methanesulphonyl chloride (300 mg.) was added to a cold solution of **3 : 4 : 5**-tri-*O*-acetyl-2-deoxy-D-glucose diethyl mercaptal (900 mg.) in dry pyridine (5 ml.), and the mixture set aside at 0°. Thereafter it was poured into ice–water (50 ml.) and extracted with chloroform (3 × 20 ml.). The combined extracts were worked up in the usual way and the resultant syrup dissolved in methanol and treated with charcoal. Concentration of the solution after removal of the charcoal gave the *product* (630 mg.) as a colourless syrup, $[\alpha]_D^{17}$ +36° (*c*, 1·82) (Found: C, 44·3; H, 6·5; S, 20·4. $C_{17}H_{30}O_9S_3$ requires C, 43·0; H, 6·3; S, 20·25%).

Action of Excess of Hydrogen Bromide on **3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-6-O-*triphenylmethyl*-D-*glucose Diethyl Mercaptal*** (XVII).—A solution of (XVII) (2·5 g.) in dry glacial acetic acid (15 ml.) was treated with a solution of hydrogen bromide (2 mol.) in dry glacial acetic acid. After 5 min. the mixture was filtered and the filtrate poured on ice and sodium hydrogen carbonate. Water was added, the solution was extracted with chloroform, and the combined extracts were worked up as described for the 2-deoxy-D-galactose analogue. A brown syrup was thereby obtained which on distillation gave a pale yellow syrup (0·5 g.), b. p. 170—175° (bath-temperature)/0·01 mm. Trituration with methanol and recrystallisation from the same solvent gave an unidentified product (0·35 g.), m. p. 73° (Found: C, 88·0; H, 7·2; S, 5·7%). Redistillation of the

compound resulted in some decomposition and yielded a syrup which crystallised from methanol. The crystals (0·05 g.) had m. p. 69—70° (Found : C, 90·9; H, 9·6%).

3 : 4 : 5-*Tri*-O-*acetyl*-2-*deoxy*-D-*glucose Diethyl Mercaptal* 6-(*Diphenyl Phosphate*) (XX).—Diphenyl phosphorochloridate (1·23 g.) was added to a chilled solution of **3 : 4 : 5**-tri-*O*-acetyl-2-deoxy-D-glucose diethyl mercaptal (3·2 g.) in dry pyridine (15 ml.), and the mixture set aside overnight at 0°. Thereafter it was poured into ice–water and worked up in the usual way. The *product* (4·4 g., 80%) was obtained as a colourless viscous syrup, n^{18} 1·5195, $[\alpha]_D^{17}$ +32° (*c*, 1·1) (Found : C, 53·3; H, 6·2; S, 10·5. $C_{38}H_{37}O_{10}PS_2$ requires C, 53·5; H, 5·9; S, 10·2%).

Attempts to remove the thio-groups from the foregoing compound gave a product which was not crystalline, contained phosphorus, but no sulphur, and restored the colour to Schiff's reagent.

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Deoxy-sugars. Part XXIX. A Further Contribution to the Chemistry of the Glycal Reaction.*

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The conversion of D-glucal into 2-deoxy-D-glucose is accompanied by a dehydration process and some 3-hydroxy-2-hydroxymethyl-2-pyran is also formed. It has been shown that treatment of glycals with ion-exchange resins in the acid form results in the production of impure 2-deoxy-sugars.

IN previous communications (Deriaz, Overend, Stacey, Teece, and Wiggins, *J.*, 1949, 1879; Overend, Shafizadeh, and Stacey, *J.*, 1951, 992; Shafizadeh and Stacey, *J.*, 1952, 3608) results obtained during a comprehensive study of the glycal reaction (cf. Helferich, *Adv. Carbohydrate Chem.*, 1952, **7**, 209) have been outlined. In addition to improving the overall yield of deoxy-sugar from the glycal, side reactions have been investigated; *e.g.*, it has been demonstrated that D-glucal on treatment with methanolic hydrogen chloride affords not only methyl 2-deoxy-αβ-D-glucoside, but also other compounds amongst which 2-hydroxymethyl-5-methoxymethylfuran was identified (Shafizadeh and Stacey, *loc. cit.*). We also have some evidence that **4 : 5**-dihydro-4-hydroxy-**2 : 5**-bismethoxymethylfuran is formed. Further examination of the products of side-reactions has led to the isolation of a pyran derivative.

Separation of 2-deoxy-D-glucose from the mixture obtained by the action of dilute sulphuric acid on D-glucal left a residue from which an ether-soluble $C_6H_8O_3$ syrup (*A*) was isolated. This unsaturated compound was recognised as 3-hydroxy-2-hydroxymethyl-2-pyran on the following evidence. The ultraviolet absorption spectrum was similar to that of furfuryl alcohol and 2-hydroxymethyl-5-methoxymethylfuran, showing a maximum absorption at 215 mμ (two conjugated double bonds; cf. Braude, *Ann. Reports*, 1945, **42**, 105). Catalytic hydrogenation resulted in the uptake of 2 mols. of hydrogen and afforded a saturated product (*B*) characterised as its crystalline bis-**3 : 5**-dinitrobenzoyl derivative. The initial compound (*A*) also afforded a crystalline di-*O*-benzoate. At this stage the possibility was considered that dilute sulphuric acid converts glucal into **2 : 5**-bishydroxymethylfuran [cf. conversion of glucal into 2-hydroxymethyl-5-methoxymethylfuran by methanolic hydrogen chloride (Shafizadeh and Stacey, *loc. cit.*)]. However, compound (*A*)

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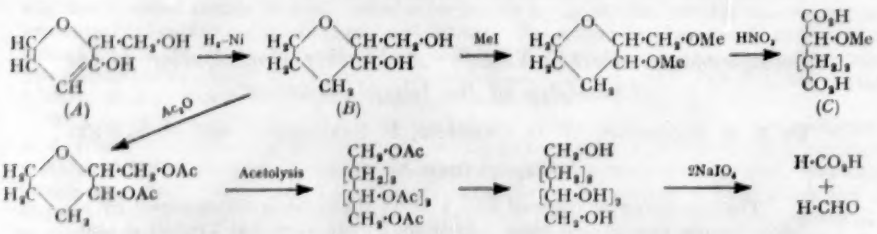
was optically active and its di-*O*-benzoate differed from that obtained from authentic 2 : 5-bishydroxymethylfuran (cf. Wiggins and Newth, *Research*, 1950, **3**, 50). Moreover, the bis-3 : 5-dinitrobenzoate of the reduction product (*B*) differed from the corresponding derivative of tetrahydro-2 : 5-bishydroxymethylfuran [prepared from hydroxymethylfurfuraldehyde (Haworth, Jones, and Wiggins, *J.*, 1945, 1)].

The di-*O*-methyl derivative of product (*B*), when treated with boiling 2N-nitric acid followed by concentrated nitric acid at 0° [conditions required for the oxidation of tetrahydrofuran and tetrahydropyran (Jones and Taylor, *Quart. Rev.*, 1950, **4**, 195) and dihydropyran (*Org. Synth.*, 1950, **30**, 48)], afforded an optically inactive methoxyglutaric acid (*C*). Acetolysis of the di-*O*-acetate of compound (*B*) (cf. Wiggins *et al.*, *loc. cit.*; Hudson *et al.*, *J. Amer. Chem. Soc.*, 1944, **66**, 1898) furnished a tetra-*O*-acetate, which on deacetylation gave a 2 : 3-dideoxyhexitol. The structure of the last compound was established by periodate oxidation : the dideoxyhexitol consumed 2 mols. of oxidant and afforded 1 mol. of formaldehyde and somewhat less than 1 mol. of formic acid (cf. Hirst and Jones, *J.*, 1949, 1659, who report a similar deficiency of formic acid on like treatment of inositol). It follows that acid (*C*) was not internally compensated, but rather that its racemic nature was responsible for the lack of optical activity, and that it was an α-methoxyglutaric acid. The sequence of reactions described may be depicted :



α-Methoxyglutaric acid (*C*) would be derived from tetrahydro-3-hydroxy-2-hydroxymethylpyran (*B*) by methylation and subsequent oxidation. Compound (*B*) would result from the hydrogenation of 3-hydroxy-2-hydroxymethylpyran (*A*). Any other sequence of conjugated double bonds in (*A*) would result in the compound's being optically inactive. Furthermore, it is a reasonable expectation that the double bond present in glucal would remain fixed, since any initial migration of this bond requires the hydroxyl group at $C_{(3)}$ to undergo an anionotropic migration to $C_{(1)}$ (cf. Braude, *Quart. Rev.*, 1950, **4**, 404); this would result in compound (*A*) having a $C_{(4)}$ double bond and a $C_{(5)}$ hydroxyl group. Such a compound would yield glutaric acid in the reactions described.

Treatment of D-galactal with dilute sulphuric acid in addition to affording 2-deoxy-D-galactose, likewise gave some of the pyran derivative (*A*), but in less amount. In this case the limited nature of the side reaction may account for the greater yields of 2-deoxy-D-galactose, compared with 2-deoxy-D-glucose, in the glycal reaction. Presumably the pyran derivative (*A*) is formed by a simple dehydration process involving the hydroxyl group adjacent to the allylic system, and this reaction proceeds more readily with glucal than with galactal.

Attempts have been made to convert glycals into deoxy-sugars by means of ion-exchange resins in acidic form (cf. Wadman, *J.*, 1952, 3051; Cadotte, Smith, and Spriestersbach, *J. Amer. Chem. Soc.*, 1952, **74**, 1501; for the use of cation-exchange resins in promoting the formation of glycosides from pentoses, hexoses, uronic acids, and methylated sugars, and of *iso*propylidene derivatives of sugars and methyl glycosides). Glucal and galactal were

treated separately with Amberlite IR-100(H) and IR-120(H). In one series of experiments the resin was packed in a cooled glass column, but since continuous re-cycling of the glycal solution was required this method was abandoned in favour of stirring the resin in a cooled aqueous solution of the glycal. The low temperatures reduced the formation of tarry materials. In all cases the progress of the reaction was followed by examining aliquot parts by paper ionophoresis (Foster, *Chem. and Ind.*, 1952, 1050). It could be demonstrated that the glycal was progressively converted to the 2-deoxy-sugar, but that undesirable side products were also formed, and that by merely evaporating a filtered solution it was not possible to obtain the deoxy-sugar crystalline. The syrupy products could be characterised by formation of the crystalline diethylmercaptals (cf. Overend, Stacey, and Staněk, *J.*, 1949, 2841). The ionophoresis results, which indicated a progressive diminution of the amount of glycal in the solution concurrent with the increase in amount of deoxy-sugar, precluded the possibility of formation of the mercaptal directly from the glycal.

Experimental

3-Hydroxy-2-hydroxymethylpyran.—(a) *From* D-*glucal.* A solution of D-glucal (25 g.) in sulphuric acid (5%; 200 c.c.) was kept at 0° for 15 hr. and then neutralised with barium hydroxide. The mixture was separated at the centrifuge, the supernatant liquid filtered through charcoal, and the filtrate concentrated to a thick syrup which was dissolved in dry methanol (4 vol.). The solution was refiltered and then evaporated to dryness and the residue treated with amyl alcohol (120 c.c.). 2-Deoxy-D-glucose (11·7 g.; m. p. 145—146°) crystallised. The mother liquors were concentrated (to 30 c.c.) and ether (60 c.c.) was then added. A resinous material was discarded. Evaporation of the remaining solution afforded a syrupy residue from which *3-hydroxy-2-hydroxymethylpyran* (3·6 g.) was obtained, b. p. 120—130° (bath temp.)/0·01 mm., n^{21} 1·507 (Found: C, 56·3; H, 6·1. $C_6H_8O_3$ requires C, 56·2; H, 6·2%).

(b) *From* D-*galactal.* D-Galactal (40 g.) was treated with ice-cold sulphuric acid, and 2-deoxy-D-galactose (35 g.) isolated as described by Overend, Shafizadeh, and Stacey (*J.*, 1951, 998). The mother liquors were concentrated (to 30 c.c.) and ether (60 c.c.) was added. Thereafter the pyran derivative (0·37 g.), $[\alpha]_D^{18}$ +15° (*c*, 7 in MeOH), was isolated as described previously. Treatment of 3-hydroxy-2-hydroxymethylpyran with benzoyl chloride and pyridine gave a good yield of *di*-O-*benzoate* as needles, m. p. 85°, $[\alpha]_D$ +64° (*c*, 1·6 in MeOH) (Found: C, 71·6; H, 4·8. $C_{20}H_{16}O_5$ requires C, 71·4; H, 4·8%).

Tetrahydro-3-hydroxy-2-hydroxymethylpyran.—A solution (30 c.c.) of 3-hydroxy-2-hydroxymethylpyran (1·189 g.) in aqueous ethanol was shaken with Raney nickel (0·7 g.) in an atmosphere of hydrogen at a slight overpressure, at room temperature. When the uptake of hydrogen was complete the filtered solution was evaporated to dryness. *Tetrahydro-3-hydroxy-2-hydroxymethylpyran* (0·91 g.) formed a syrup, n^{19} 1·478 (Found: C, 54·9; H, 8·9. $C_6H_{12}O_3$ requires C, 54·5; H, 9·1%). The *3 : 5-dinitrobenzoyl* derivative had m. p. 172° (Found: C, 46·0; H, 3·0; N, 10·8. $C_{20}H_{16}O_{13}N_4$ requires C, 46·1; H, 3·1; N, 10·8%).

Tetrahydro-3-methoxy-2-methoxymethylpyran.—To tetrahydro-3-hydroxy-2-hydroxymethylpyran (3 g.) in liquid ammonia (250 c.c.), sodium (1·6 g.) was added portionwise slowly. The mixture was stirred under anhydrous conditions for 6 hr. and then methyl iodide (4·3 c.c.) was added. This procedure was repeated four times and then the product was isolated in the usual fashion. *Tetrahydro-3-methoxy-2-methoxymethylpyran* (2·4 g.) formed a liquid, b. p. 100° (bath temp.)/12 mm., n^{18} 1·437 (Found: C, 60·0; H, 10·0; OMe, 38·3. $C_8H_{16}O_3$ requires C, 60·0; H, 10·0; OMe, 38·7%).

Oxidation of Tetrahydro-3-methoxy-2-methoxymethylpyran.—The tetrahydropyran (2·1 g.) and 0·2N-nitric acid (6 c.c.) were heated at 100° for 2 hr. Thereafter the product was cooled in ice–salt and gradually added to ice-cold nitric acid (*d*, 1·42; 9 g.) containing sodium nitrite (0·1 g.). The mixture was stirred continuously at 0° for 2 hr. before the temperature was slowly raised to that of the room. When the solution became pale yellow it was diluted with water and evaporated under diminished pressure. This procedure was repeated until most of the excess of nitric acid had been removed. The syrupy residue was dissolved in water, neutralised with potassium hydrogen carbonate, and re-evaporated. The dry residue was extracted with dry methanol and after concentration (to 10 c.c.) the extract was heated under reflux for 8 hr. with methyl iodide (5 c.c.). After removal of solvents the residue was extracted with warm ether. The residue from this extraction was re-treated with dry methanol and methyl iodide and again

extracted with ether. The combined ethereal extracts were evaporated and the syrupy residue was distilled. Besides starting material (0·47 g.) [b. p. 110—120° (bath temp.)/15 mm.], racemic *dimethyl α-methoxyglutarate* (0·9 g.) was obtained, b. p. 125—135° (bath temp.)/0·05 mm., n^{19} 1·4459 (Found: C, 50·9; H, 7·6. $C_8H_{14}O_5$ requires C, 50·5; H, 7·4%).

3-Acetoxy-2-acetoxymethyltetrahydropyran.—A solution of tetrahydro-3-hydroxy-2-hydroxymethylpyran (2·63 g.) in a mixture of dry pyridine (10 c.c.) and freshly distilled acetic anhydride (15 c.c.) was kept at 0° for 3 days. Thereafter the product was isolated according to the standard procedure and *3-acetoxy-2-acetoxymethyltetrahydropyran* (3·7 g.) was obtained; it had b. p. 183° (bath temp.)/15 mm., n^{21} 1·4465 (Found: C, 55·2; H, 7·6. $C_{10}H_{14}O_5$ requires C, 55·5; H, 7·4%).

This di-*O*-acetate (3·5 g.) was dissolved in a mixture of acetic anhydride (35 c.c.), glacial acetic acid (15 c.c.), and concentrated sulphuric acid (1 c.c.) at 0°. The mixture was kept at room temperature for 10 days and was then poured into ice-water and extracted with chloroform. The extract was washed successively with sodium hydrogen carbonate solution and water, dried ($MgSO_4$), and evaporated to dryness. From the residue there was obtained a *1 : 4 : 5 : 6-tetra-O-acetyl-2 : 3-dideoxyhexitol* (4 g.), b. p. 170° (bath temp.)/0·02 mm., n^{24} 1·4436 (Found: C, 52·6; H, 7·1. $C_{14}H_{22}O_8$ requires C, 52·8; H, 6·9%).

2 : 3-Dideoxyhexitol.—1 : 4 : 5 : 6-Tetra-*O*-acetyl-2 : 3-dideoxyhexitol (1·5 g.) was added to barium hydroxide (6·2 g.) in water (40 c.c.) and the mixture was heated at 90° for 2 hr. After addition of solid carbon dioxide the mixture was centrifuged and then filtered, the filtrate was evaporated to dryness, and the residue was extracted with methanol. Evaporation of the extract yielded a *2 : 3-dideoxy-DL-hexitol* (0·4 g.) as a hygroscopic syrup, b. p. 220—225° (bath temp.)/0·02 mm., n^{24} 1·495 (Found: C, 47·8; H, 9·4. $C_6H_{14}O_4$ requires C, 48·0; H, 9·3%). A solution of this compound (25·4 mg.) in water (5 c.c.) was treated with sodium metaperiodate (0·075M, 10 c.c.) and water was added to give a final volume of 25 c.c. At intervals, aliquot parts (2 c.c.) were withdrawn and the uptake of oxidant determined. Likewise the amounts of formic acid and formaldehyde produced during the oxidation were estimated. The latter was weighed as its dimedone derivative (m. p. 189—190°), and it was shown that 1·15 mol. of formaldehyde were formed. 2-Deoxy-D-sorbitol behaved as expected in control experiments as a model compound.

Treatment of Glycals with Ion-exchange Resins.—D-Glucal (1 g.) in water (50 c.c.) was passed 25 times through a column (65 cm. × 15 mm.) of Amberlite resin IR-120(H) (30 g.) which was cooled to 1—2°. The resin was washed with water (200 c.c.), and the combined eluate and washings were concentrated and then examined by ionophoresis (apparatus as described by Foster, *Chem. and Ind.*, 1952, 1050). It was demonstrated that the amount of D-glucal decreased progressively during the cyclisation process and the amount of 2-deoxy-D-glucose correspondingly increased. Essentially similar results were obtained by using IR-100(H) resin. In neither case could the syrup obtained on evaporation of the solutions be induced to crystallise satisfactorily.

In another experiment D-glucal (1 g.) was stirred for 3 hr. at 0° with Amberlite resin IR-120 (H) (20 g.) in water (50 c.c.). Samples were examined every 15 min. ionophoretically. After 3 hr. the glucal had been practically completely converted into 2-deoxyglucose. Evaporation of the solution afforded a syrup which would not crystallise, but readily afforded 2-deoxy-D-glucose diethylmercaptal (0·25 g.) as white plates, m. p. and mixed m. p. 134—135°, on treatment with ethanethiol (2 c.c.) and hydrochloric acid (1·25 c.c.).

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Pristimerin. Part I.

By R. C. Shah, A. B. Kulkarni, and V. M. Thakore.

[Reprint Order No. 5350.]

On the basis of elementary analyses and molecular-weight determinations, pristimerin, isolated by Bhatnagar and Divekar (*J. Sci. Ind. Res., India*, 1951, **10**, *B*, 56), has been assigned a provisional molecular formula $C_{28}H_{36}O_4$ (Kulkarni and Shah, *Nature*, 1954, **173**, 1237). Its quinonoid character is indicated by its rapid decolorisation by reducing agents and the reappearance of the colour on aeration, and has been confirmed by reductive acetylation. Its solubility in alcoholic sodium hydrogen sulphite and concomitant decolorisation suggest the presence of a β-quinonoid grouping (Fieser, *J. Amer. Chem. Soc.*, 1926, **48**, 2925). However, in view of a negative test with *o*-phenylenediamine an α-quinonoid structure cannot be excluded. It gives a positive test with boroacetic anhydride (Dimroth and Foust, *Ber.*, 1921, **54**, 3020; *Annalen*, 1925, **446**, 97; cf. Anderson *et al.*, *Analyt. Chim. Acta*, 1952, **7**, 226), suggesting the presence of a potential hydroxy-group probably *peri* to the quinone grouping. It contains one methoxy-group and gives no active hydrogen (Zerewitinoff), the last observation being confirmed by the absence of a hydroxyl band in the infrared spectrum. Methylated pristimerin contains three methoxy-

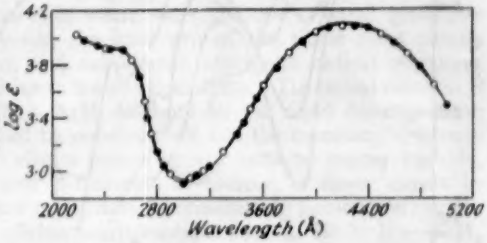

Fig. 1. *Ultraviolet absorption of* (○—○) *primisterin* (0·0263 *g./l.*) *and* (●—●) *methylcelastrol* (0·03252 *g./l.*), *both in* 95% EtOH.

groups, so during its preparation disproportionation has taken place; the ring containing the quinone grouping is aromatised and the two hydroxy-groups so formed are methylated (Sheshadri *et al.*, *Proc. Indian Acad. Sci.*, 1948, **27**, *A*, 245). This trimethyl ether forms a 2 : 4-dinitrophenylhydrazone and therefore has a keto-group which must presumably be present also in pristimerin. The presence of the keto-group is confirmed by the reduction of the trimethyl ether with lithium aluminium hydride to a compound $C_{30}H_{44}O_4$ which does not form a ketonic derivative and has an infrared hydroxyl band (3350 $cm.^{-1}$). Thus the nature of all the oxygen atoms in pristimerin is established. Titration with perbenzoic acid shows the presence of one double bond in the trimethyl ether.

Pristimerin has the characteristic ultraviolet absorption of a quinone (Fig. 1), and this curve is identical with that of methylcelastrol (Gisvold, *J. Amer. Pharm. Assoc.*, 1939, **28**, 449; 1940, **29**, 12; 1942, **31**, 529; Fieser and Jones, *ibid.*, 1942, **31**, 315; Schechter and Haller, *J. Amer. Chem. Soc.*, 1942, **64**, 182). The identity of the substances is confirmed by the melting point and mixed melting point. The ultraviolet absorption curves of reductively acetylated pristimerin (Fig. 2*A*) and methylated pristimerin (Fig. 2*B*) show the presence of a substituted benzene ring system (cf. Fig. 2*C*; Morton and Sawires, *J.*, 1940, 1052; Campbell and Coppingen, *J. Amer. Chem. Soc.*, 1951, **73**, 2708) and not that of a substituted naphthalene (Fig. 2*D* and *E*) or a higher aromatic fused-ring system. These observations lead us to believe that pristimerin is a benzoquinone derivative (Brockmann and Budde, *Ber.*, 1953, **86**, 432). The molecular formula $C_{22}H_{30}O_3$ and the naphthaquinone structure assigned to celastrol, therefore, appear to be untenable.

Experimental.—Purification of pristimerin. Crude pristimerin (5 g.), m. p. 214°, crystallised from benzene–light petroleum (1 : 1) in orange-red stout needles (3·6 g.), m. p. 216—217°. For analysis it was crystallised six times, then having m. p. 219—220°, and its homogeneity was confirmed by chromatographic adsorption on silicic acid and quantitative elution therefrom

[Found : C, 77·4, 77·5, 77·0; H, 8·4, 8·6, 8·9; OMe, 8·1; *C*-Me, 7·2%; *M*, (cryoscopic in C_6H_6) 391, (*X*-ray method) 429. $C_{28}H_{36}O_4$ requires C, 77·2; H, 8·3; OMe, 7·1; 2*C*-Me, 6·9%; *M*, 436]. The *compound* gives a greenish-brown colour with alcoholic ferric chloride; it is insoluble in alkali but its yellow alcoholic solution on addition of alkali or acid becomes deep red. It has absorption max. in 95% EtOH at 2440 (ε 8320), 2560 (ε 7890), and 4250 Å (ε 12,270).

Reductive acetylation. To a boiling solution of pristimerin (135 mg.) in acetic anhydride (25 c.c.) zinc dust was added until it became colourless. After filtration the excess of anhydride was removed under a vacuum and the residue was extracted with chloroform. The extract was washed with water, aqueous sodium carbonate, and water, dried (Na_2SO_4), and evaporated. The residual *acetate* crystallised from alcohol as colourless needles (85 mg.), m. p. 245—246° after two further crystallisations (Found : C, 74·0, 74·4; H, 8·2, 8·2; OMe, 5·9; Ac, 12·9, 13·3. $C_{32}H_{42}O_6$ requires C, 73·6; H, 8·1; OMe, 5·9; Ac, 16·5%), $[\alpha]_D^{22}$ +105·9° (*c* 0·0604 in $CHCl_3$), $\lambda_{max.}$ 2660—2760 Å (ε 775) in 95% EtOH.

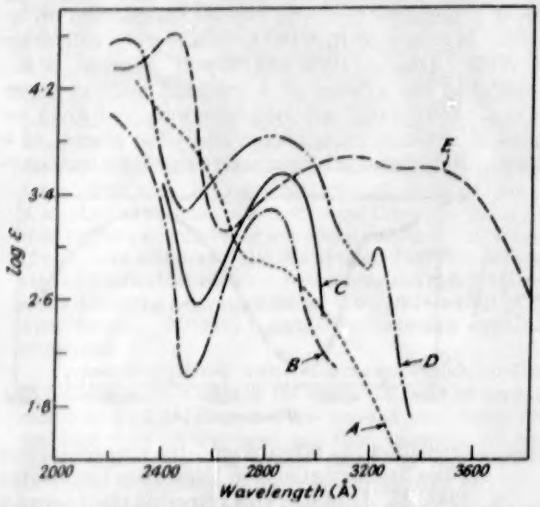

FIG. 2. *Ultraviolet absorption of* (*A*) *the product* (0·05017 *g./l.*) *of reductive acetylation of primisterin,* (*B*) *methylated primisterin* (0·0675 *g./l.*), (*C*) 1 : 2 : 4-*trimethoxybenzene* (0·0682 *g./l.*), (*D*) 1 : 2 : 4-*triacetoxynaphthalene* (0·0632 *g./l.*) (*A*—*D in* 95% EtOH), *and* (*E*) 1 : 2 : 4-*trihydronaphthalene* (from Daglish, *J. Amer. Chem. Soc.*, 1950, **72**, 4859).

Methylation. Pristimerin (140 mg.) was refluxed in acetone with methyl sulphate (2 c.c.) and potassium carbonate (1 g.) for 3 hr. Then more methyl sulphate (2 c.c.) was added and the solution was further refluxed for 3 hr. Acetone was removed, the mixture diluted with water, and the *ether* filtered off. It (130 mg.), m. p. 170—175°, was crystallised from dilute alcohol, giving long colourless needles (83 mg.), m. p. 184—185° (Found : C, 77·2; H, 9·6; OMe, 20·4; active H, 0. $C_{30}H_{42}O_4$ requires C, 77·3; H, 9·0; 3OMe, 19·9%). It consumes 0·77 atom-equiv. of oxygen on titration with perbenzoic acid, gives a negative ferric chloride test but a positive test with tetranitromethane, and has an absorption max. at 2840 Å (ε 1900) in 95% EtOH. The 2 : 4-*dinitrophenylhydrazone* forms needles (from alcohol), m. p. 206° (decomp.; shrinking at 189°) (Found : C, 66·8; H, 7·5; N, 7·9. $C_{36}H_{46}O_7N_4$ requires C, 66·6; H, 7·1; N, 8·7%).

Reduction of methylated pristimerin with lithium aluminium hydride. Methylated pristimerin (115 mg.) in ether (50 c.c.) was added to lithium aluminium hydride (120 mg.) in ether (50 c.c.) and then worked up as usual. The residual *alcohol* crystallised from alcohol as colourless needles (45 mg.), m. p. 162° (decomp.) (Found : C, 76·4; H, 10·1; OMe, 17·3. $C_{30}H_{44}O_4$ requires C, 76·8; H, 9·4; 3OMe, 19·9%).

The authors are grateful to Colonel S. S. Bhatnagar for supplying pristimerin, to Professor J. D. Bernal for determining the molecular weight by *X*-rays and to Mr. W. Manser, of Edg. Techn. Hochschule, Zurich, for checking and confirming some of the microanalytical results obtained at Poona. They also thank Professor Gisvold for a sample of methylcelastrol.

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Organosilicon Compounds. Part XIV. The Reaction between Trisubstituted Silanes and Silver Perchlorate.*

By C. Eaborn.

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Triorganosilanes and silver perchlorate react in toluene solution with precipitation of silver and evolution of hydrogen. The material balance is represented roughly by:

$$R_3SiH + AgClO_4 \longrightarrow R_3SiClO_4 + Ag + \tfrac{1}{2}H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

but deviations from this of as much as 20% in the yields of hydrogen and silver are common. The amount of silver formed is always low, but for a given silane is greater the greater the relative initial concentration of silver perchlorate (Runs 8 and 10, 14 and 15, 22 and 25); and when silver perchlorate is initially in excess the amount of hydrogen is lower the greater this excess (Runs 1—5, 6—12, 14—15). With an initial deficiency of silver salt the amount of hydrogen produced is usually more than equivalent to the silver salt (Run 1), and sometimes more than equivalent to the organosilane taken (Runs 16, 25, 26, 27).

Exact conclusions are impossible because apparently duplicate reactions sometimes gave amounts of hydrogen differing by as much as 15%, although the rates of gas evolution from such "duplicates" usually agreed well during the first 50—60% of reaction. The discrepancies seemed not to be due to traces of water, since addition of small quantities of water had no apparent effect. However, the hydrogen of the silane must almost certainly be initially liberated as atoms, and subsequent atom and radical reactions, possibly of the chain type, would be sensitive to traces of catalysts. The initial reaction is probably $AgClO_4 + R_3SiH \longrightarrow R_3SiClO_4 + AgH$, followed by the rapid decomposition $AgH \longrightarrow Ag + \cdot H$. [The two steps could be simultaneous, but the transitory existence of silver hydride is proposed because (i) silanes reduce copper salts to copper hydride, and (ii) when silanes are mixed with silver perchlorate in toluene, or silver nitrate in ethanol or aqueous acetone, a golden-yellow precipitate is immediately formed and rapidly becomes black as hydrogen is evolved.] Subsequent reactions such as $H\cdot + \cdot H \longrightarrow H_2$ (normally accounting for some 80—100% of the reaction), $Ag^+ + \cdot H \longrightarrow Ag + H^+$, $R_3SiH + \cdot H \longrightarrow R_3Si\cdot + H_2$, along with attack of atoms or radicals on the solvent, could account for the departures from the stoicheiometry of eqn. (1).

With triethylsilane, at a fixed initial concentration of silver salt, the initial rate of hydrogen evolution is roughly proportional to the initial concentration of silane (Runs 1—5), while at a fixed silane concentration (Runs 6—13) this rate is proportional to the square of the silver salt concentration up to 0·35M (but the fall in the rate of hydrogen evolution as reaction proceeds is usually markedly less than expected for a third-order reaction). Above this, increase in the silver salt concentration causes even greater rise in the initial rate than would be expected for an order of two with respect to this salt. Reaction is faster in the less polar solvent benzene (Runs 31 and 32).

For the silanes examined (except possibly the unreactive tri*iso*propylsilane and the very reactive tribenzylsilanes, which cannot be accurately studied) the plots of volume of hydrogen against log time are roughly superimposable, implying that the mechanism of the reactions does not seriously vary. The reactivities of the R_3SiH compounds, as revealed by the initial rate of hydrogen evolution, lie in the following series, the figures in parentheses showing the approximate relative reactivities within each set: (R_3=) Et_3 (1) > Pr^n_3 (0·5) > Bu^n_3 (0·35) > Bu^i_3 (0·013) > Pr^i_3 (0·001); (p-C_6H_4Me)Me_2 (1·1) > Ph, Me_2 (1); (p-$C_6H_4Me)_3$ (3·8) > Ph_3 (1) > (p-$C_6H_4Cl)_3$ (0·2); (p-Me·C_6H_4·$CH_2)_3$ (1·2) > (C_6H_4·$CH_2)_3$ (1) > (p-C_6H_4Cl·$CH_2)_3$ (0·03); (C_6H_4·$CH_2)_3$ (~200) > Ph, Me_2 (~40) > Et_3 (1) > Ph_3 (0·04).

The very low reactivity of the sterically hindered tri*iso*propylsilane implies that nucleophilic attack on silicon is involved in the initial (rate-determining) breaking of the Si–H bond, even though the strongest nucleophile present is perchlorate ion. However, the

* Part XIII, *J.*, 1955, 2047.

special effectiveness of silver ions in decomposing silanes strongly indicates that electrophilic attack on hydrogen is important, and since electron-release in R raises the reactivity of R_3SiH the electrophilic attack predominates in the transition state. Simultaneous attack of perchlorate ion on silicon and silver ion on hydrogen would account for the order of two with respect to silver perchlorate. The higher rate in a less polar solvent would be expected for such a reaction, involving disappearance of ionic charges.

Experimental.—Toluene was dried by long storage over phosphoric oxide. Silver perchlorate was dried at 120° for 24 hr., and weighed samples were re-dried at 120° for several hours immediately before use.

Triethylsilane and silver perchlorate. It was considered unsafe to attempt isolation of triethylsilyl perchlorate.

(i) A solution of silver perchlorate (41·5 g.) in toluene (350 ml.) was added during 6 hr. to a solution of triethylsilane (24 g.) in toluene (250 ml.). After an additional 20 hr. the mixture was stirred with water, and the silver (20 g., 90% based on triethylsilane) was filtered off. The toluene layer was washed with dilute alkali and water and then dried (Na_2SO_4), and the toluene was fractionally distilled from the mixture. The residue was distilled, to give 1·0 g. of liquid of b. p. 140—220° [Et_3SiOH + $(Et_3Si)_2O$ (?)], and 23 g. (90%) of hexaethyldisiloxane, b. p. 225—235°, n_D^{17} 1·4350, leaving a small residue (*ca.* 0·5 ml.) which ignited.

(ii) The gas from triethylsilane (0·01 mole) and silver perchlorate (0·015 mole) in toluene (20 ml.) was shown by mass-spectral analysis to contain 99 vol. % of hydrogen (the remaining 1% being reported as carbon dioxide).

Rate studies. The reactants were put into the separate arms of a twin-limbed vessel, which was immersed in a thermostat (23·2° ± 0·02°) and connected to a manometer; the solvent used in the reaction was used also as manometric liquid. When the system reached equilibrium (*ca.* ½ hr.) the vessel was shaken in such a way that all the liquid ran into any one limb once every second. When gas evolution ceased the silver was filtered off and determined by titration after dissolution in nitric acid.

The following typical runs with triethylsilane (initially 0·00093 mole) show the rates of gas evolution at different initial silver perchlorate concentrations: (*a*) 0·00252, (*b*) 0·00155, (*c*) 0·000774 mole. The gas volume was measured over toluene at 18°/738 mm. The volume of the reaction mixture was 7 ml.

(*a*) Time (min.)	0	½	1	1½	2	3	4	5	7	10	15	26	∞
H_2 (ml.)	0	0·40	1·05	1·73	2·21	3·18	4·00	4·69	5·71	6·86	8·03	9·29	10·3

(*b*) Time (min.)	0	1	2	4	7	12	18	28	38	83	∞
H_2 (ml.) ...	0 *	0·27	0·68	1·47	2·52	3·97	5·20	6·69	7·85	10·36	12·0

* —0·1 when reactants were mixed.

(*c*) Time (min.)	0	1	2	4	8	16	28	41	63	98	142	183
H_2 (ml.)	0	0·05	0·16	0·36	0·76	1·58	2·71	3·77	5·10	6·48	7·54	8·31

The following list gives, in order, the number of the run (in parentheses), R_3 in R_3SiH, the initial amount of silane, the initial amount of perchlorate, the amount of hydrogen evolved, the amount of silver precipitated (all quantities in units of 10^{-5} mole) and (in italics) the initial rate of hydrogen evolution in ml. at N.T.P. per min. The volume of the reaction mixture was 7 ml. except for runs 23, 24, and 26—30, in which it was 12 ml.

(1), Et_3, 180, 155, 66, —, *0·75*; (2), Et_3, 90, 155, 48·1, —, *0·39*; (3), Et_3, 72, 155, —, —, *0·31*; (4), Et_3, 54, 155, 27·0, —, *0·19*; (5), Et_3, 36, 155, 14·2, —, *0·11*; (6), Et_3, 93, 337, 39·1, —, *2·94*; (7), Et_3, 93, 301, —, —, *2·03*; (8), Et_3, 93, 266, 40·6, 90·0, *1·51*; (9), Et_3, 93, 252, 40·8, —, *1·11*; (10), Et_3, 93, 216, 46·0, 85·0, *0·82*; (11), Et_3, 93, 155, 47·6, —, *0·40*; (12), Et_3, 93, 117, 48·0, —, *0·21*; (13), Et_3, 93, 77·2, —, —, *0·089*; (14), Bu^n_3, 100, 216, 52·3, 79·7, *0·32*; (15), Bu^n_3, 100, 301, 50·5, 89·3, *0·68*; (16), Pr^n_3, 100, 216, 53·5, 79·2; *0·43*; (17), Bu^i_3, 100, 301, —, —, *0·024*; (18), Pr^i_3, 100, 301, —, —, *ca. 0·0016*. In 22 hr., $4·3 \times 10^{-5}$ mole of hydrogen and 17×10^{-5} g.-atom of silver were formed; the latter figure is probably high because of exposure of the reaction mixture to moisture during filtration; (19), Ph_3, 100, 301, 50·0, 90·2, *0·076*; (20), $(p\text{-}C_6H_4Me)_3$, 100, 301, 37·0, 95·7, *0·29*; (21), $(p\text{-}C_6H_4Cl)_3$, 100, 301, —, —, *0·015*; (22), $(C_6H_5{\cdot}CH_2)_3$, 100, 301, 50·0, 98·4, — (too fast to follow); (23), Ph,Me_2, 100, 155, 47·4, 78·8, *3·6*; (24), Et_3, 100, 155, 49·0, —, *0·085*; (25), $(C_6H_5{\cdot}CH_2)_3$, 100, 77·2,

54·1, 75·8, *>5*; (26), $(C_6H_5{\cdot}CH_2)_3$, 100, 77·2, 60·0, —, *~4·5*; (27), $(p\text{-}Me{\cdot}C_6H_4{\cdot}CH_2)_3$, 100, 77·2, 55·2, —, *~5·6*; (28), $(p\text{-}C_6H_4Cl{\cdot}CH_2)_3$, 100, 77·2, —, —, *0·16*; (29), Ph, Me_3, 100, 77·2, —, —, *0·85*; (30), $(p\text{-}Me{\cdot}C_6H_4)Me_2$, 100, 77·2, —, —, *0·98*; (31), Et_3, 80, 119 (supersaturated), 47·7, —, *0·33* (in benzene); (32), Et_3, 80, 85·3, 46·0, —, *0·20* (in benzene).

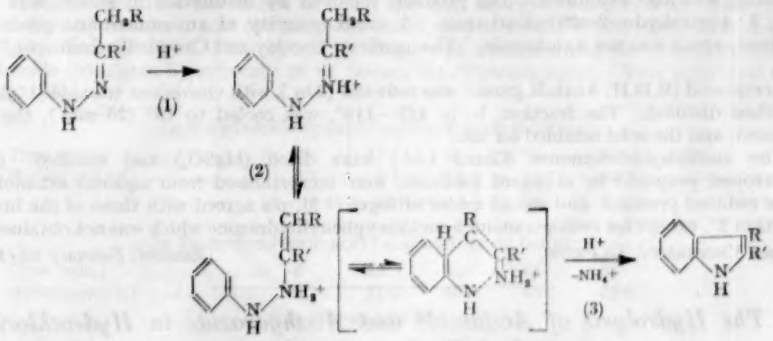
UNIVERSITY COLLEGE, LEICESTER. [*Received, January 25th*, 1955.]

Some Kinetic Observations on the Fischer Indole Reaction.

By JAMES MCLEAN, STEWART MCLEAN (in part), and ROWLAND I. REED.

[Reprint Order No. 6100.]

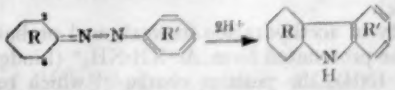
THE suggested mechanism of the Fischer indole reaction (Carlin and Fisher, *J. Amer. Chem. Soc.*, 1948, **70**, 3421; Carlin, Wallace, and Fisher, *ibid.*, 1952, **74**, 990) is shown below in an abridged form. Carlin (*ibid.*, p. 1077) has further examined this mechanism with reference



to Pausacker and Schubert's kinetic measurements (*J.*, 1950, 1814), and has considered the case in which reaction (3) is the slow, rate-determining stage.

The above sequence, with reaction (2) as the rate-determining process, is also consistent with the known kinetic evidence. Moreover it is not necessary that the slow stage be the same under all experimental conditions.

The measured first-order rate constants for the formation of a series of substituted tetrahydrocarbazoles in acetic acid are as follows



R	R′	[Hydrazone]	Temp.	10^5k_1 (sec.$^{-1}$)	R	R′	[Hydrazone]	Temp.	10^5k_1 (sec.$^{-1}$)
H	H	0·024	35·0°	2·62	H	H	0·089	35·0°	2·81
,,	,,	0·031	,,	2·80	,,	,,	0·188	,,	2·81 [a]

R	R′	[Hydrazone]	Temp.	10^5k_1 (sec.$^{-1}$)	$k_{(6)}$	$k_{(8)}$	R	R′	[Hydrazone]	Temp.	10^5k_1 (sec.$^{-1}$)
H	H	0·033	40·9°	4·59	2·30	2·30	H	*p*-MeO	0·033	40·0°	—
4-Me	,,	,,	,,	4·41	2·20	2·20	,,	*p*-Me	,,	,,	36·8
3-Me	,,	,,	,,	3·30	—	3·30	,,	H	,,	,,	4·07
2-Me	,,	,,	,,	40·8	36·4 [b]	4·4	,,	*o*-Me	,,	,,	7·67

[a] Value interpolated from Pausacker and Schubert's data (*J.*, 1950, 1814) is 2·58. [b] This product is tetrahydro-11-methylcarbazolenine.

$k_{(6)}$ and $k_{(8)}$ are the partial rate constants for position 2 and 6, respectively.

The ring-closure of 2-methyl*cyclo*hexanone phenylhydrazone in acetic acid as solvent gives largely tetrahydro-11-methylcarbazolenine, whilst with aqueous sulphuric acid there is about twice as much 1 : 2 : 3 : 4-tetrahydro-1-methylcarbazole as of this basic product. These results support those of Pausacker (*J.*, 1950, 621) which suggest that the ratio of possible products varies with the solvent. The heterogeneous nature of the reactions in

aqueous sulphuric acid would not affect this conclusion if, as is probable, both reaction sequences have protonation as a common origin.

Experimental.—The kinetic measurements were made by dilatometric methods, tapless dilatometers (Benford and Ingold, *J.*, 1938, 925) being used, and ammonia estimations by the standard micro-Kjeldahl method (Pausacker and Schubert, *J.*, 1950, 1814). In view of the uncertainties attached to the former method, it was frequently checked by the second at one or more points. Generally the two methods agreed and the value determined from the dilatometric estimation (Guggenheim, *Phil. Mag.*, 1926, 538) was preferred. The extent of the reaction was also determined in many cases, the values lying between 60 and 80% of the theoretical.

Ring closure of the 2-methyl*cyclo*hexanone phenylhydrazone in aqueous sulphuric acid was by Pausacker's method (*J.*, 1950, 623). The yields of 1 : 2 : 3 : 4-tetrahydro-1-methylcarbazole and tetrahydro-11-methylcarbazolenine were 50% and 28%, respectively; the values for the experiment in acetic acid were 7% and 61% of the theoretical.

The ring-closure of the 3-methyl*cyclo*hexanone derivative, which could give rise to two products, was also examined. The product, removed by distillation in steam, was mainly 1 : 2 : 3 : 4-tetrahydro-2-methylcarbazole. A small quantity of an unidentified product was obtained, which was not a carbazole. This confirms Barclay and Campbell's findings (*J.*, 1945, 530).

Acetic acid (B.D.H. AnalaR grade) was refluxed (2 hr.) with chromium trioxide (1% by wt.), and then distilled. The fraction, b. p. 117—118°, was cooled to 15° (20 min.), the liquid decanted, and the solid retained for use.

The methyl*cyclo*hexanones (Glaxo Ltd.) were dried ($MgSO_4$) and distilled. Phenylhydrazones, prepared by standard methods, were recrystallised from aqueous ethanol, dried under reduced pressure, and stored under nitrogen. M. p.s agreed with those of the literature to within 2°, except for *cyclo*hexanone *p*-methoxyphenylhydrazone which was not obtained pure.

THE UNIVERSITY, GLASGOW. [*Received, February 7th,* 1955.]

The Hydrolysis of Acetamide and Acethydrazide in Hydrochloric Acid of Various Concentrations.

By J. T. EDWARD, H. P. HUTCHISON, and S. C. R. MEACOCK.

[Reprint Order No. 6147.]

IN connection with a problem in protein chemistry, the stability of acethydrazide to hydrochloric acid at 61° has been compared with that of acetamide. The hydrolysis of both compounds in excess of acid followed first-order kinetics. The hydrazide was hydrolyzed more slowly than the amide in acid weaker than about 2·5N but more rapidly in stronger acid (see Table).

The greater stability of acethydrazide in weak acid probably comes in part from the fact that it exists in the protonated form, $Ac{\cdot}NH{\cdot}NH_3^+$ (Lindgren and Niemann, *J. Amer. Chem. Soc.*, 1949, **71**, 1504), the positive charge of which repels hydrogen ions and so protects the compound from acid-catalysed hydrolysis (cf. Butterworth, Eley, and Stone, *Biochem. J.*, 1953, **53**, 30). As the ionic strength increases, this effect operates less strongly (La Mer, *Chem. Rev.*, 1932, **10**, 179).

First-order rate constants for the hydrolysis of acethydrazide (H) *and acetamide* (A) *in hydrochloric acid.*

Normality of acid	1·0	1·5	2·0	2·5	3·0	3·5	4·0	5·0	7·0	8·0
H : 10^3k (min.$^{-1}$)	0·49	1·08	1·53 [a]	2·62 [b]	2·69 [a]	—	—	—	6·5	—
A : 10^3k (min.$^{-1}$)	1·27 [c]	1·66	—	2·20	2·30	2·11	1·91 [d]	1·71	—	—[e]

[a] Mean of two determinations. [b] Mean of three determinations.

Interpolation of Arrhenius plots of Rabinovitch and Winkler's results (*Canad. J. Res.*, 1942, **20**, *B*, 73) gives [c] $k = 1{\cdot}32 \times 10^{-3}$ min.$^{-1}$; in the same way, [d] $k = 1{\cdot}90 \times 10^{-3}$ min.$^{-1}$, and [e] $k = 0{\cdot}52 \times 10^{-3}$ min.$^{-1}$.

The maximum rate for the hydrolysis of acetamide at 61° was found in about 3N-hydrochloric acid, the concentration found previously for maximum rates at 50° (Taylor, *J.*, 1930, 2741) and 25° (Krieble and Holst, *J. Amer. Chem. Soc.*, 1938, **60**, 2976; Taylor, *loc. cit.*).

Experimental.—Materials. Acetamide was recrystallized from acetone to a constant m. p. of 82°, and acethydrazide (Curtius and Hofmann, *J. prakt. Chem.*, 1896, **53**, 524) from chloroform to a constant m. p. of 67°.

Analytical method for acethydrazide. This was based on the blue complex formed between cupric ion and hydrazides (Aggarwal, Darbari, and Rây, *J.*, 1929, 1941; Fallab and Erlenmeyer, *Helv. Chim. Acta*, 1953, **26**, 6). The blue colour given by acethydrazide in 0·5M-cupric nitrate was measured in a Lange colorimeter against the cupric nitrate solution as a blank, using a white-light source. Beer's law was obeyed for concentrations of acethydrazide up to 0·031M. When the cupric nitrate was 0·5N with respect to hydrochloric acid, hydrazine or acetic acid in concentrations up to 0·036M did not interfere with the determinations.

Rate measurements. (*a*) Acethydrazide. Acethydrazide in a thin glass bulb was added to hydrochloric acid (50 ml.) in a stoppered flask in a thermostat at 61·0° ± 0·2°. The mixture was stirred vigorously to break the bulb and cause the acethydrazide to dissolve. At intervals samples (*ca.* 6 ml.) were withdrawn and cooled rapidly. To an aliquot part (5 ml.), standard sodium hydroxide solution was added to bring the acid strength down to 0·5N; 0·5M-cupric nitrate in 0·5N-hydrochloric acid (30 ml.) was added, and sufficient 0·5N-hydrochloric acid to give a final volume of 70 ml. The optical densities were measured and the concentrations of acethydrazide calculated by reference to an empirical calibration curve. Two individual runs are illustrated:

In N-hydrochloric acid; acethydrazide 0·366M.

Time (min.)	9	21	40	74	98	121
Hydrolysis (%)	2·2	5·5	15·1	27·7	36·9	56·6

$k = 0{\cdot}49 \times 10^{-3}$ min.$^{-1}$.

In 2N-hydrochloric acid; acethydrazide 0·405M.

Time (min.)	5	19	32	44	56
Hydrolysis (%)	8·7	27·3	40·0	49·0	58·0

$k = 1{\cdot}54 \times 10^{-2}$ min.$^{-1}$.

(*b*) Acetamide. The same procedure was followed as for acethydrazide, the hydrolysis being followed by formol titration (Northrop, *J. Gen. Physiol*, 1926, **9**, 767) of the ammonia produced.

We are grateful to Professor W. Cocker for his constant encouragement, and one of us (S. C. R. M.) thanks the government of the Republic of Ireland and the Medical Research Council of Ireland for maintenance grants.

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The Preparation of [^{14}C]*Ethylenediamine Dihydrochloride from* [1-^{14}C]*Ethanol.*

By D. S. POPPLEWELL and R. G. WILKINS.

[Reprint Order No. 6179.]

FOR exchange studies of metal–ethylenediamine complexes, it was necessary to synthesise [^{14}C]ethylenediamine dihydrochloride. A highly active product was not desired and so it was possible to avoid synthesis on a small carrier-free scale with its attendent difficulties (Thomas and Turner, *Quart. Rev.*, 1953, **7**, 408).

Diluted [1-^{14}C]ethanol was catalytically dehydrated and [^{14}C]ethylene, obtained in 75—80% yields, absorbed in bromine to form 1 : 2-dibromo[^{14}C]ethane. Dehydration by any of the chemical methods (*e.g.*, hot syrupy phosphoric acid) gave poor yields (cf. Fries and Calvin, *J. Amer. Chem. Soc.*, 1948, **70**, 2235). [^{14}C]Ethylenediamine dihydrochloride was obtained from 1 : 2-dibromo[^{14}C]ethane by a modified Gabriel synthesis in hot *NN*-dimethylformamide (Sheehan and Bolhofer, *J. Amer. Chem. Soc.*, 1950, **72**, 2786) followed by the usual hydrazine hydrate treatment (Ing and Manske, *J.*, 1926, 2348). The use of the solvent in the formation of 1 : 2-diphthalimidoethane gave higher yields (80—85%)

than the usual method (*e.g.*, Putochim, *Chem. Abs.*, 1930, **24**, 3756, reported 60%). The yield for the complete conversion averaged 50—55%.

[$^{14}C_2$]Ethylene has previously been obtained in excellent yields on a microscale by reduction of [$^{14}C_2$]acetylene (Arrol and Glascock, *J.*, 1949, 5335; Yattargolis, Klimenok, and Golsvina, *Doklady Akad. Nauk S.S.S.R.*, 1952, **86**, 313; Cox and Warne, *J.*, 1951, 1893).

Experimental.—*1 : 2-Dibromo*[^{14}C]*ethane.* [1-^{14}C]Ethanol (0·1 mc; 2·3 mg.; supplied by Radiochemical Centre, Amersham) was mixed thoroughly with dried redistilled inactive ethanol (2·86 g.) and heated gently in a 15-c.c. round-bottomed flask connected by a side-arm to a tube, 17" long, packed with dried activated alumina (Type H, 100—200 mesh; Peter Spence and Sons Ltd.) and heated electrically at 360—400°. The emerging gas containing [^{14}C]ethylene passed into an absorption vessel containing bromine (12 g.) and fitted with a bubble-spiral so as to ensure good contact between the rising gas and the bromine. The time taken to evaporate the ethanol was about 150 min. and after this a slow stream of nitrogen was passed through the apparatus for about 5 min. The product in the absorption vessel was shaken thoroughly with several portions of 2N-sodium hydroxide until the latter no longer showed a red colour. 1 : 2-Dibromo[^{14}C]ethane remained (8·8 g.) and was dried and used in the next stage.

1 : 2-Diphthalimido[^{14}C]*ethane.* 1 : 2-Dibromo[^{14}C]ethane (8·3 g.), recrystallised potassium phthalimide (20 g.), and dimethylformamide (90 c.c.) were heated on a steam-bath for 4 hr. with occasional swirling. The bulk of the solvent was removed and the residue cooled in ice. The solid was filtered off and washed well with water, leaving an almost white solid (7·45 g.; m. p. 228—232°). A further amount of less pure product (4·3 g.; m. p. 195—215°) was obtained on concentration of the filtrate. The combined amount was boiled with carbon disulphide to extract any 2-bromo-1-phthalimidoethane and the residue (11·7 g.) used in the next stage. A small amount, recrystallised from absolute alcohol, had m. p. 233° (Found: C, 67·5; H, 3·7; N, 8·4. Calc. for $C_{18}H_{12}O_4N_2$: C, 67·7; H, 3·7; N, 8·8%). 1 : 2-Diphthalimidoethane prepared from ethylenediamine and phthalic anhydride (Wanag, *Ber.*, 1942, **75**, 719), had m. p. 233° alone or mixed with above product.

[^{14}C]*Ethylenediamine dihydrochloride.* Crude 1 : 2-diphthalimido[^{14}C]ethane (11·7 g.), suspended in absolute alcohol (300 c.c.), was treated with a slight excess of hydrazine hydrate (3·3 g.), and the suspension gently refluxed. After about 45 min. a clear solution was obtained and after a further 15 min. a white flocculent precipitate suddenly appeared in large amount. Heating was continued for a further 2—3 hr. The alcohol was evaporated, and the residual solid heated at about 100° for 15 min. under reduced pressure to remove any excess of hydrazine, and then refluxed with hydrochloric acid (1 : 1; 100 c.c.) for a further 3 hr. The acid was removed by heat under reduced pressure. The buff-coloured residue was lixiviated with small amounts of ice-cold water, the extract was evaporated to dryness, and the residue (4·9 g.) washed with a little hot absolute alcohol and recrystallised from concentrated hydrochloric acid (yield, 4·3 g.) (Found: C, 18·9; H, 7·65; Cl, 53·7. Calc. for $C_2H_{10}N_2Cl_2$: C, 18·1; H, 7·5; Cl, 53·4%). The picrate had m. p. and mixed m. p. 233°.

Radiochemical yield. Weighed amounts of the diluted [^{14}C]ethanol and [^{14}C]ethylenediamine dihydrochloride were separately quantitatively oxidised to [^{14}C]carbon dioxide by the Van Slyke–Folch combustion fluid (*J. Biol. Chem.*, 1940, **136**, 509). The evolved gas was collected in a small volume of carbon dioxide-free 2N-sodium hydroxide and converted into barium [^{14}C]-carbonate, weighed amounts of which were mounted on filter paper discs and their activity was measured. Standard counting equipment was used in conjunction with an end-window Geiger–Müller counter. Activities were reduced to those for an "infinitely thin" sample in the usual way (Cook and Duncan, "Modern Radiochemical Practice," Oxford Univ. Press, 1952, p. 234). It was found that under identical conditions the [^{14}C]barium carbonate activity was (from [^{14}C]-ethanol) $1{\cdot}89 \times 10^6$ counts min.$^{-1}$ mmole^{-1} and (from [^{14}C]ethylenediamine dihydrochloride) $1{\cdot}87 \times 10^6$, indicating that the overall radiochemical yield was the same as the chemical one, namely 52%.

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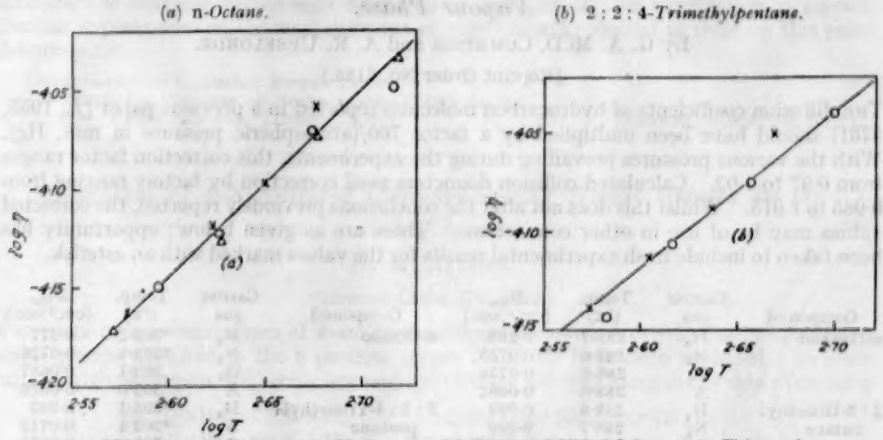
THE UNIVERSITY, SHEFFIELD, 10. [*Received, February 28th*, 1955.]

The Viscosity of the Vapours of n-*Octane and* 2 : 2 : 4-*Trimethylpentane.*

By G. A. McD. Cummings and J. C. McCoubrey.

[Reprint Order No. 6187.]

McCoubrey, McCrea, and Ubbelohde have reported (*J.*, 1951, 1961) measurements of the viscosity of a number of hydrocarbon vapours. The importance of the viscosity of C_8 isomers in fuel problems has prompted us to make fresh measurements on *n*-octane and 2 : 2 : 4-trimethylpentane, higher vapour pressures being used in the same apparatus in an



△ Melaven and Mack. × McCoubrey, McCrea, and Ubbelohde. ○ This work.

attempt to obtain more accurate data for the viscosity of these vapours. The new data are combined with those already available (McCoubrey *et al.*, *loc. cit.*; Melaven and Mack, *J. Amer. Chem. Soc.*, 1932, **54**, 888) to obtain the best values.

The combined measurements over the whole range of temperatures have been correlated by the following equations :

(1) $\log \eta = s \log T + c$ with a standard deviation Δ, where η is the viscosity in c.g.s. units, T is the temperature in °K, and s and c are constants.

(2) $$\eta = 0{\cdot}086\rho\bar{c}/NA\ (1 + C/T)$$

where ρ is the density, $\bar{c}$ is the root-mean-square velocity, C is Sutherland's constant, and A is Sutherland's collision area in Å^2 (Chapman and Cowling, " Mathematical Theory of Non-uniform Gases," Cambridge Univ. Press, 1939).

(3) $$\eta = 266{\cdot}93(MT)(r_0)^{-2}\ V/W(2)$$

where M is the molecular weight, r_0 is the low-velocity collision diameter of the Lennard-Jones intermolecular potential

$$E(r) = 4\varepsilon[(r_0/r)^{12} - (r_0/r)^6]$$

and V and $W(2)$ are tabulated functions of ε, the depth of the potential well (Hirschfelder, Curtiss, and Bird, " Molecular Theory of Gases and Liquids," John Wiley, New York, 1954).

Values of the constants for the above equations obtained from calculated lines of closest fit are given in the Table. The Figures show the scatter of individual points from different experimental sources in the case of the log η–log T plots.

	n-Octane	2 : 2 : 4-Trimethylpentane		*n*-Octane	2 : 2 : 4-Trimethylpentane
s	0·944	0·915	A (Å^2) ...	31·5	31·6
c	−6·599	−6·501	ε/k	337	279
Δ	0·002	0·004	r_0 (Å)	7·38	7·48
C	376	342			

No significant alteration in the conclusions drawn in the previous paper (McCoubrey *et al., loc. cit.*) is necessitated by the new measurements.

The authors thank Professor A. R. Ubbelohde for permission to publish these results obtained in his laboratory, and for advice on the problem.

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Collision Diameters of Flexible Hydrocarbon Molecules in the Vapour Phase.

By G. A. McD. CUMMINGS and A. R. UBBELOHDE.

[Reprint Order No. 6188.]

THE diffusion coefficients of hydrocarbon molecules reported in a previous paper (*J.*, 1953, 3751) should have been multiplied by a factor 760/(atmospheric pressure in mm. Hg). With the various pressures prevailing during the experiments, this correction factor ranges from 0·97 to 1·03. Calculated collision diameters need correction by factors ranging from 0·985 to 1·015. Whilst this does not alter the conclusions previously reported, the corrected values may be of use in other connections. These are as given below; opportunity has been taken to include fresh experimental results for the values marked with an asterisk.

Compound	Carrier gas	Temp. (°K)	D_{760} (cm.²/sec.)	Compound	Carrier gas	Temp. (°K)	D_{760} (cm.²/sec.)
n-Hexane	H_2	288·7	0·288	*n*-Octane	H_2	*303·2	0·277
	N_2	288·6	0·0753		N_2	*303·1	0·0726
	O_2	288·6	0·0754		O_2	303·1	0·0687
	A	288·6	0·0662		A	303·0	0·0626
2 : 3-Dimethyl-butane	H_2	288·8	0·299	2 : 2 : 4-Trimethyl-pentane	H_2	*303·1	0·292
	N_2	288·7	0·299		N_2	*303·1	0·0713
	O_2	288·4	0·0742		O_2	303·0	0·0672
	A	288·9	0·0652		A	303·0	0·0605
*cyclo*Hexane ...	H_2	288·5	0·319	*n*-Decane	H_2	363·8	0·293
	N_2	288·6	0·0746		N_2	*363·9	0·0763
	O_2	288·6	0·0731	2 : 3 : 3-Trimethyl-heptane	H_2	363·9	0·271
	A	288·7	0·0721		N_2	363·8	0·0681
Methyl*cyclo*-pentane	H_2	288·5	0·312	*n*-Dodecane	H_2	399·6	0·311
	N_2	285·9	0·0758		N_2	399·4	0·0829
	O_2	287·1	0·0744				
	A	288·6	0·0715				

Apparent collision diameters of hydrocarbons (σ_D).

Compound	Carrier : H_2	N_2	$\Delta(\sigma_{H_2} - \sigma_{N_2})$	O_2	A
n-Hexane	6·78	6·51	+0·27	6·39	6·59
2 : 3-Dimethylbutane	6·60	6·53	+0·07	6·43	6·67
*cyclo*Hexane	6·30	6·58	−0·28	6·52	6·20
Methyl*cyclo*pentane	6·40	6·42	−0·02	6·46	6·18
n-Octane	7·31	6·94	+0·37	7·01	7·02
2 : 2 : 4-Trimethylpentane	7·05	7·02	+0·03	7·14	7·21
n-Decane	8·46	8·08	+0·38	—	—
2 : 3 : 3-Trimethylheptane	8·91	8·75	+0·16	—	—
n-Dodecane	8·91	8·37	+0·54	—	—

As pointed out in other publications, large " hydrogen effects " appear to be associated with molecular flexibility. In this connection, the rôle of ethylene is at present a matter for controversy, since diffusion diameters determined by different experimental techniques (Trautz and Müller, *Ann. Physik*, **1935**, **22**, 350, 371; Boyd, Stein, Steingrimsson, and Rumpel, *J. Chem. Phys.*, 1951, **19**, 548) do not agree (see Table). On the other hand, the

Collision diameters for ethylene calculated from observed mass-diffusion experiments.

Carrier gas	Trautz and Müller	Boyd *et al.*
H_2	4·80	4·12
N_2	3·67	4·18
$(H_2 - N_2)$	+1·13	−0·06

theoretical expectations for ethylene are not yet fully worked out. Hydrogen is markedly more efficient than nitrogen for promoting the transfer from translational to vibrational energy in collisions with ethylene. The number of collisions $Z_{eff.}$ for one act of transfer for hydrogen = 250, $Z_{eff.}$ for nitrogen >3500 (Richards and Reid, *J. Chem. Phys.*, 1934, **2**, 206; McGrath and Ubbelohde, *Proc. Roy. Soc.*, 1954, **227**, *A*, 1). However, for molecular encounters to show " roughness " in the Pidduck sense, thus affecting collision parameters for momentum or mass transfer, it seems probable that $Z_{eff.}$ must be still smaller than either of the above values. There should be no appreciable difference between the diffusion diameters of ethylene mixed with hydrogen or nitrogen if this expectation is correct. Further experiments on the mass diffusion of ethylene are required to clear up this point definitely.

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Syntheses of 8-Substituted Quinolines with Amide Groups in the Side Chain.

By M. NEEMAN.

[Reprint Order No. 6189.]

A NUMBER of new derivatives of 8-amino-6-methoxyquinoline with side chains containing amide groups attached to the 8 position (types I and II) have been prepared. In comparison with pamaquin, the secondary and the tertiary nitrogen atom of the side chain have

(I) Q·NH·CO·CRR′·NEt$_2$ Q·NH·CRR′·[CH$_2$]$_n$·CO·NEt$_2$ (II)

R$_1$, R$_2$ = alkyl or H; Q = 6-methoxy-8-quinolyl; n = 0—2.

severally been acylated. The substances of type (I) were prepared from 8-amino-6-methoxyquinoline by treatment with α-halogenoacyl halides and subsequently with diethylamine, and compounds of type (II) by condensing the diethylamides of α-, β-, or γ-halogenoacids with 8-amino-6-methoxyquinoline at 100°. In these syntheses, the yields ranged from 50 to 70%.

Biological tests on a number of such compounds have been reported (Wiselogle, " A Survey of Antimalarial Drugs," J. W. Edwards, Ann Arbor, Mich., 1946; Coatney, Cooper, Eddy, and Greenberg, " Survey of Antimalarial Agents," Public Health Monograph No. 9, Federal Security Agency, U.S. Public Health Service, 1953). Our substances show toxicities of the order of that of quinine, and low or negligible antiplasmodial activity. *NN*-Diethyl-γ-(6-methoxy-8-quinolylamino)valeramide (II; R = H, R′ = Me, n = 2) had a quinine equivalent of 0·2 in a suppressive test on ducks infected with *Plasmodium lophurae* (Wiselogle, *op. cit.*, SN 5883): *N*-acetylpamaquin (SN 12,448) also has a lower toxicity than pamaquin, and negligible antiplasmodial activity.

Experimental.—8-(α-Halogenoacylamido)-6-methoxyquinolines were prepared by the action of α-halogenoacyl chlorides or bromides (1 equiv.) on 8-amino-6-methoxyquinoline (1 equiv.) in chloroform with cooling. The hydrohalides of the products were precipitated as yellow to reddish-brown substances and were either recrystallised as such or converted into the corresponding bases.

8-Chloroacetamido-6-methoxyquinoline crystallised as white needles (from ethanol or ligroin), m. p. 112° (U.S.P. 2,494,083 reported m. p. 110—111°).

8-α-*Bromopropionamido-6-methoxyquinoline monohydrobromide*, crystallised from 30% aqueous hydrobromic acid, had m. p. 180° (Found: N, 7·0. $C_{13}H_{13}O_2N_2Br$,HBr requires N, 7·2%).

8-α-*Bromo-β-methylbutyramido-6-methoxyquinoline* crystallised from ethanol as white needles, m. p. 104° (Found: C, 53·5; H, 5·2. $C_{15}H_{17}O_2N_2Br$ requires C, 53·4; H, 5·1%). The *monohydrobromide* crystallised from 30% aqueous hydrobromic acid as yellow needles, m. p. 185° (Found: C, 43·5; H, 4·3; N, 6·7. $C_{15}H_{17}O_2N_2Br$,HBr requires C, 43·1; H, 4·3; N, 6·7%).

8-(α-*NN*-Diethylaminoacylamido)-6-methoxyquinolines (I) were prepared by refluxing the

corresponding 8-α-halogenoacylamido-6-methoxyquinolines with excess of diethylamine for 20—48 hr. Excess of amine was distilled off, and the residue was treated with aqueous sodium hydroxide, extracted with ether, and distilled under reduced pressure. Thus were obtained: 8-(α-*NN*-Diethylaminoacetamido)-6-methoxyquinoline (I; R = R′ = H), a yellow oil, b. p. 200—215°/1 mm. (U.S.P. 2,494,083 reported b. p. 260—263/35 mm.), n_D^{26} 1·5852 [the *dihydrochloride*, precipitated from acetone by concentrated aqueous hydrochloric acid, crystallised from ethanolic hydrochloric acid as brown needles, m. p. 214—216° (Found: C, 53·4; H, 6·3. $C_{16}H_{21}O_2N_3,2HCl$ requires C, 53·3; H, 6·4%)]. *8-(α-NN-Diethylamino-β-methylbutyramido)-6-methoxyquinoline* (I; R = H, R′ = Pr^i), white needles, m. p. 262° (decomp.) (Found: C, 69·6; H, 8·2; N, 12·5. $C_{19}H_{27}O_2N_3$ requires C, 69·3; H, 8·3; N, 12·75%).

The compounds (II) were prepared by the action of the diethylamides of the appropriate α-, β-, or γ-halogeno-acids in slight excess on 8-amino-6-methoxyquinoline at 100°, for 3—30 hr. and crystallised directly from the corresponding aqueous hydrohalogen acid or were isolated as base.

The required diethylamides were prepared at −5° by the action of α-, β-, or γ-halogenoacyl chlorides or bromides in dry ether on 2 equivs. of diethylamine. After 3 hr., the diethylamine hydrochloride was filtered off, and the filtrate freed from solvent and distilled under reduced pressure, yielding *NN*-diethyl-α-chloroacetamide, b. p. 133°/30 mm. (Jacobs and Heidelberger, *J. Biol. Chem.*, 1915, **21**, 145, reported b. p. 126·5—128·5°/21 mm.; Hahn and Loos, *Ber.*, 1918, **51**, 1436, reported b. p. 190—195°/25 mm.), n_D^{21} 1·4690 (Found: Cl, 23·4. Calc. for $C_6H_{12}ONCl$: Cl, 23·7%). *-β-chloropropionamide*, b. p. 92°/2 mm., n_D^{16} 1·4698, d^{16} 1·0451, $[M_R]_D$ 43·69 (calc., 43·34) (Found: Cl, 22·0. $C_7H_{14}ONCl$ requires Cl, 21·7%), and *-α-bromo-α-methylpropionamide*, b. p. 86°/2·5 mm., n_D^{13} 1·4878, d^{13} 1·255, $[M_R]_D$ 50·95 (calc., 50·86) (Found: Br, 35·7. $C_6H_{12}ONBr$ requires Br, 36·0%).

NN-Diethyl-γ-chlorovaleramide. *NN*-Diethylævulamide was reduced by aluminium *iso*propoxide in propan-2-ol (Haskelberg, *J. Amer. Chem. Soc.*, 1948, **70**, 2830), and the product was treated with thionyl chloride in benzene. After 1 hour's refluxing, excess of thionyl chloride and solvent was removed. The product distilled as a colourless oil, b. p. 94°/2 mm. (Wohlgemuth, *Ann. Chim.*, 1914, **2**, 302, reported b. p. 139—140°/17 mm.) (Found: C, 56·0; H, 9·3. Calc. for $C_9H_{18}ONCl$: C, 56·4; H, 9·5%).

NN-Diethyl-α-(6-methoxy-8-quinolylamino)acetamide dihydrochloride (II; R = R′ = H, *n* = 0), crystallised from dilute aqueous hydrochloric acid, had m. p. 230° (decomp.) (Found: C, 53·3; H, 6·0. $C_{16}H_{21}O_2N_3,2HCl$ requires C, 53·3; H, 6·4%). The base was obtained as white crystals, m. p. 228° (U.S.P. 2,456,911 reported b. p. 175—180°/48 mm.). The *monopicrate* crystallised from ethanol as dark yellow crystals, m. p. 198° (Found: N, 16·2. $C_{16}H_{21}O_2N_3,C_6H_3O_7N_3$ requires N, 16·3%).

NN-Diethyl-α-(6-methoxy-8-quinolylamino)propionamide (II; R = Me, R′ = H, *n* = 0) crystallised as white needles (from butanol), m. p. 202° (Found: N, 13·6. $C_{17}H_{23}O_2N_3$ requires N, 13·9%). The *dihydrochloride* crystallised in orange crystals (from aqueous-ethanolic hydrochloric acid), m. p. 217° (Found: C, 54·8; H, 6·5. $C_{17}H_{23}O_2N_3,2HCl$ requires C, 54·55; H, 6·7%).

NN-Diethyl-β-(6-methoxy-8-quinolylamino)propionamide (II; R = R′ = H, *n* = 1), b. p. 250°/2 mm., yielded the *dihydrochloride* by precipitation from a solution in ethyl acetate by ethanolic hydrochloric acid and recrystallisation from water as orange crystals, m. p. 230° (Found: C, 54·5; H, 6·5%).

NN-Diethyl-α-(6-methoxy-8-quinolylamino)-α-methylpropionamide (II; R = R′ = Me, *n* = 0) crystallised in colourless hexagonal plates (from benzene), m. p. 220°. The *monohydrochloride* crystallised as brown needles (from dilute aqueous hydrochloric acid), m. p. 244° (decomp.) (Found: N, 12·2. $C_{18}H_{25}O_2N_3,HCl$ requires N, 11·9%).

NN-Diethyl-γ-(6-methoxy-8-quinolylamino)valeramide (II; R = Me, R′ = H, *n* = 2) distilled as a yellow viscous oil, b. p. 225—230°/0·06 mm., 160°/0·01 mm., which crystallised from light petroleum as yellow needles, m. p. 79° (Found: C, 68·9; H, 7·9; N, 13·0. $C_{19}H_{27}O_2N_3$ requires C, 69·3; H, 8·3; N, 12·75%). The *hydrochloride* prepared from the base by addition of aqueous hydrochloric acid recrystallised from water formed a hydrate, m. p. 128°, which lost water at 100°/30 mm. over phosphoric oxide. The resulting salt had m. p. 167° (Found: C, 62·5; H, 8·0. $C_{19}H_{27}O_2N_3,HCl$ requires C, 62·4; H, 7·7%).

The author expresses his gratitude to the late Dr. L. Haskelberg of the Daniel Sieff Research Institute, Rehovoth, for his advice and help.

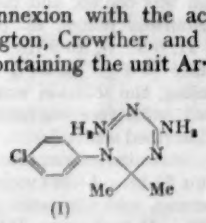
Research Council of Israel, Jerusalem. [*Received, March 2nd*, 1955.]

1 : 2-*Dihydro*-2 : 2-*dimethylquinazolines. The Condensation of Acetone with Anthranilamide Derivatives.*

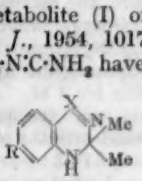
By H. C. CARRINGTON.

[Reprint Order No. 6227.]

IN connexion with the active metabolite (I) of the antimalarial drug Paludrine (see Carrington, Crowther, and Stacey, *J.*, 1954, 1017), dihydroquinazolines (II; X = NH_2), also containing the unit Ar·N·CMe_2·N:C·NH_2 have been prepared for the first time. They



(I)



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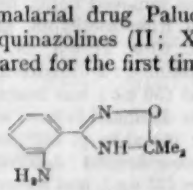

(III)

are readily obtained by condensing *o*-aminobenzamidines with acetone in acid aqueous solution. Similarly anthranilamide and acetone give 1 : 2-dihydro-4-hydroxy-2 : 2-dimethylquinazoline (II; R = H, X = OH) (alternatively formulated as 1 : 2 : 3 : 4-tetrahydro-2 : 2-dimethyl-4-oxoquinazoline). The corresponding thioamide gives the 4-thiol (II; R = H, X = SH). The relation between these compounds is demonstrated by the following reactions. The compound (II; R = H, X = NH_2) is converted by acid hydrolysis into the hydroxy-compound (II; R = H, X = OH). The thiol (II; R = H, X = SH) with methyl iodide gives the methylthio-derivative (II; R = H, X = SMe), which is converted by alcoholic ammonia into the amine (II; R = H, X = NH_2).

o-Aminobenzamidine was prepared from *o*-aminobenzonitrile by addition of hydroxylamine to give the amidoxime (Pinnow and Sämann, *Ber.*, 1896, **29**, 623) and reduction of this. The amidoxime does not react with acetone in a similar way to the other anthranilic acid derivatives, but behaves in the way common to amidoximes, giving the oxadiazole (III).

4-Amino-7-chloro-1 : 2-dihydro-2 : 2-dimethylquinazoline (II; X = NH_2, R = Cl) was similarly prepared. Neither it nor its parent showed antimalarial activity.

Experimental.—1 : 2-*Dihydro*-4-*mercapto*-2 : 2-*dimethylquinazoline.* A solution of 2-aminothiobenzamide (Reissert and Grube, *Ber.*, 1909, **42**, 3710) (1·52 g.) in 3·5% hydrochloric acid (20 c.c.) and acetone (20 c.c.) was heated under reflux on the steam-bath for 18 hr. The yellow crystalline solid which separated on cooling recrystallised from aqueous methanol, to give the *quinazoline derivative* (1·8 g.), m. p. 151—152° (Found: C, 62·4; H, 6·05; N, 14·5. $C_{10}H_{12}N_2S$ requires C, 62·6; H, 6·25; N, 14·6%).

1 : 2-*Dihydro*-2 : 2-*dimethyl*-4-*methylthioquinazoline.* 1 : 2-Dihydro-4-mercapto-2 : 2-dimethylquinazoline (2 g.) in ether (150 c.c.) was allowed to stand overnight with methyl iodide (2 c.c.). The gum which separated was extracted with water, and the extract was clarified and made alkaline to Brilliant-yellow with ammonia. The yellow precipitate was washed with water, dried, and crystallised from light petroleum (b. p. 40—60°), giving the *methylthio-derivative* (1 g.), m. p. 62—64° (Found: C, 64·4; H, 6·6; N, 13·8. $C_{11}H_{14}N_2S$ requires C, 64·1; H, 6·8; N, 13·6%).

o-*Aminobenzamidine.* *o*-Aminobenzamidoxime (8 g.) in ethanol was reduced by hydrogen in presence of Raney nickel at 65°/30 atm. for 5 hr. After cooling and removal of the catalyst the hydrochloride of the product was precipitated by dry hydrogen chloride. The crude product (4·6 g.), m. p. 236—242°, could not readily be purified, and was used directly for the next stage. The *picrate*, from an aqueous solution of the hydrochloride and picric acid and crystallised from ethanol, had m. p. 222—224° (Found: C, 43·0; H, 3·4; N, 22·2. $C_7H_9N_3,C_6H_3O_7N_3$ requires C, 42·9; H, 3·3; N, 22·0%).

4-*Amino*-1 : 2-*dihydro*-2 : 2-*dimethylquinazoline hydrochloride.* (*a*) *o*-Aminobenzamidine hydrochloride (8·5 g.), hydrochloric acid (*d* 1·18; 4·3 c.c.), acetone (50 c.c.), and water (100 c.c.) were heated under reflux for 15 hr. After evaporation to a small bulk under reduced pressure, the yellow solid was separated and crystallised from ethanol, to give the *quinazoline hydrochloride* (3·4 g.), m. p. 255—256° (Found: C, 56·6; H, 6·4; N, 19·3. $C_{10}H_{12}N_2$,HCl requires C, 56·7; H, 6·6; N, 19·9%).

(*b*) 1 : 2-Dihydro-2 : 2-dimethyl-4-methylthioquinazoline (5 g.) was heated with saturated ethanolic ammonia (50 c.c.) at 150° for 6 hr. After evaporation, the residual oil was dissolved in

ethanol (20 c.c.) and dry hydrogen chloride was passed into the solution until it was acid to Congo-red. Addition of ether precipitated the hydrochloride of the aminoquinazoline, which after crystallisation had m. p. 255—256° (1·9 g.) and was identical with that described under (*a*).

1 : 2-*Dihydro*-4-*hydroxy*-2 : 2-*dimethylquinazoline*.—(*a*) Anthranilamide (2·7 g.), 3·5% hydrochloric acid (40 c.c.), and acetone (40 c.c.) were heated under reflux for 15 hr. The excess of acetone was removed under reduced pressure, the residual solution was cooled, and the solid crystallised from methanol, giving the *hydroxyquinazoline* as colourless plates, m. p. 262° (Found: C, 67·9; H, 6·8; N, 16·2. $C_{10}H_{12}ON_2$ requires C, 68·2; H, 6·8; N, 15·9%).

(*b*) 4-Amino-1 : 2-dihydro-2 : 2-dimethylquinazoline hydrochloride (5·0 g.) in 20% hydrochloric acid (50 c.c.) was heated under reflux for 4 hr. After cooling, the solution was made alkaline to Brilliant-yellow with ammonia, and the precipitated solid recrystallised from methanol; it had m. p. 262°, and was identical with the material described under (*a*).

3-*o*-*Aminophenyl*-4 : 5-*dihydro*-5 : 5-*dimethyl*-1 : 2 : 4-*oxadiazole*. *o*-Aminobenzamidoxime (2 g.), acetone (25 c.c.), and water (50 c.c.) were heated under reflux for 24 hr. After evaporation under reduced pressure the oily residue was triturated with acetone, and the solid *product* recrystallised from acetone–ethanol–light petroleum (b. p. 40—60°). It had m. p. 214—216° (Found: C, 63·2; H, 6·8; N, 22·3. $C_{10}H_{13}ON_3$ requires C, 62·85; H, 6·8; N, 22·0%).

2-*Amino*-4-*chlorobenzamidoxime*. To a mixture of 2-amino-4-chlorobenzonitrile (13·8 g.) (McKee, McKee, and Bost, *J. Amer. Chem. Soc.*, 1947, **69**, 940) in ethanol (30 c.c.) and hydroxylamine hydrochloride (10 g.) in water (20 c.c.) was added a solution of sodium (3·6 g.) in ethanol (55 c.c.) and the whole was heated under reflux for 8 hr. The ethanol was removed under reduced pressure and the residue was made alkaline to Clayton-yellow with dilute aqueous sodium hydroxide. After thorough shaking, the mixture was filtered, the filtrate was neutralised with acetic acid and cooled, and the solid product was separated. The *amidoxime*, crystallised from aqueous ethanol, had m. p. 128—130° (10·2 g.) (Found: C, 45·2; H, 4·4; N, 22·8. $C_7H_8ON_3Cl$ requires C, 45·3; H, 4·3; N, 22·6%).

2-*Amino*-4-*chlorobenzamidine dihydrochloride*. 2-Amino-4-chlorobenzamidoxime (10 g.) in ethanol (10 c.c.) was hydrogenated as above. The *dihydrochloride*, crystallised from ethanol–light petroleum, had m. p. 280—281° (11 g.) (Found: C, 34·6; H, 4·3; N, 17·8. $C_7H_8N_3Cl,2HCl$ requires C, 34·6; H, 4·1; N, 17·3%).

4-*Amino*-7-*chloro*-1 : 2-*dihydro*-2 : 2-*dimethylquinazoline*. 2-Amino-4-chlorobenzamidine dihydrochloride (5 g.), acetone (30 c.c.) and water (60 c.c.) were heated under reflux for 24 hr. After evaporation under reduced pressure the residue was made just alkaline to Clayton-yellow with dilute aqueous alkali. The yellow precipitate crystallised from aqueous ethanol, giving the *quinazoline derivative*, m. p. 198—200° (4·1 g.) (Found: C, 56·9; H, 5·8; N, 19·9. $C_{10}H_{13}N_3Cl$ requires C, 57·1; H, 5·7; N, 20·0%).

I thank Mr. J. H. Sherwood for expert technical assistance.

IMPERIAL CHEMICAL (PHARMACEUTICALS) LTD., HEXAGON HOUSE, BLACKLEY, MANCHESTER, 9.

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The Heat of Formation of Nickel Carbonyl.

By K. W. SYKES and S. C. TOWNSHEND.

[Reprint Order No. 6236.]

RECENT survey of the very discordant values so far obtained for the heat of formation of nickel carbonyl (Spice, Staveley, and Harrow, *J.*, 1955, 100) included the result of an indirect determination communicated privately by the Mond Nickel Company. A brief description of this work may be useful.

We measured the rate of formation of nickel carbonyl from carbon monoxide and nickel powder at a series of temperatures. The metal was prepared by reduction of the oxide in hydrogen and contained 0·022% of added sulphur, a known catalyst for the carbonyl reaction. A gas containing 95% of carbon monoxide was passed at 5 l. (760 mm.; 18°) per hour over nickel powder (7·86 g.) resulting in the following conversions:

Temp.	50°	104°	114°	125°	136°
Ni converted (g./hr.)	1·60	0·60	0·36	0·20	0·06

It was important to find out whether these figures represented rates of reaction or equilibrium concentrations. The only method available was to calculate ΔE_0^0 as follows. A

lower limit, C, for the equilibrium constant $K = p_{Ni(CO)_4}/p_{CO}^4$ was calculated from the expression $C = x(1{\cdot}053 - \frac{3}{4}x)^3/(1 - x)^4P^3$, where x is the fraction of carbon monoxide which has reacted and P is the total pressure (1 atm.). Free-energy functions $G^0 - E_0^0$ then available ("Selected Values of Chemical Thermodynamic Properties," Nat. Bur. Standards; Crawford and Cross, *J. Chem. Phys.*, 1938, **6**, 525) gave the following figures:

Temp.	50°	104°	114°	125°	136°
C (atm.$^{-3}$)	0·871	0·093	0·046	0·023	0·062
$\Delta(G^0 - E_0^0)/T$ (cal.)	91·81	92·90	93·09	93·27	93·41
$-\Delta E_0^0$ (kcal.)	29·57	33·25	33·66	34·13	34·08

The increase of the calculated energy of formation from 50° to 114° indicated that equilibrium, though not attained, was approached more closely as the temperature was raised; its constancy, within the experimental accuracy, at 125° and 136° suggested that equilibrium was effectively achieved at those temperatures. ΔE_0^0 was thus estimated to be −34·1 kcal. and the corresponding standard heat of formation of gaseous nickel carbonyl to be given by ΔH^0 (298° K) = −36·5 kcal. for this system. Though the lower limit should be more reliable than the upper one because equilibrium was approached only from the carbon monoxide side, the probable error is thought to be ±0·8 kcal., owing chiefly to an uncertainty of 2% in the free-energy function for nickel carbonyl. The difference of 0·2 kcal. from Spice, Staveley, and Harrow's value (*loc. cit.*) arises from the fact that the inert gas in the carbon monoxide was not previously taken into account.

Experimental.—Nickel oxide (0·038% Fe, 0·004% S), prepared by oxidising in air at 750° nickel powder (particle size 9 μ) obtained by decomposition of the carbonyl, was mixed with 0·2% of powdered $NiSO_4,7H_2O$. 10 g. of the mixture, contained as a layer 5" long in a 13 mm. Pyrex tube, were reduced in hydrogen at 370°. Process gas (92% CO) was purified in a train consisting of a nickel tube at 220°, alkaline pyrogallol, potassium hydroxide, calcium chloride, and anhydrone; the product contained 95% of carbon monoxide, the remainder being nitrogen and hydrogen. This gas was passed over the reduced nickel powder at the specified temperature and the carbonyl determined by decomposition in a weighed nickel tube maintained at 220°.

UNIVERSITY COLLEGE OF SWANSEA, UNIVERSITY OF WALES.
THE MOND NICKEL COMPANY LIMITED, CLYDACH.
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The Direct Interaction of N*-Bromosuccinimide and Benzoyl Peroxide.*

By M. C. FORD.

[Reprint Order No. 6238.]

THE homolytic chain reaction first proposed by Bloomfield (*J.*, 1944, 118) as a mechanism for the allylic bromination of olefins with *N*-bromosuccinimide requires the initial presence of a small concentration of free succinimidyl radicals, $(C_4H_4O_2)N\cdot$, these being assumed to arise by thermal or photochemical dissociation of the bromo-imide. Karrer and Schmid (*Helv. Chim. Acta*, 1946, **29**, 573) showed that traces of benzoyl peroxide catalyse the reaction, it being now generally assumed that this effect is due to the much more efficient initial generation of succinimidyl radicals by a metathetic process:

$$(Ph\cdot CO_2)_2 \longrightarrow Ph\cdot + CO_2 + Ph\cdot CO_2\cdot \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$(C_4H_4O_2)N\cdot Br + Ph\cdot \longrightarrow (C_4H_4O_2)N\cdot + Ph\cdot Br \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Although there seems to be no direct evidence for the above sequence of reactions in the case of benzoyl peroxide, the mechanism by which aliphatic azo-compounds, RR′CX·N:N·CXRR′ (R and R′ = alkyl, X = CN or CO_2Me), catalyse allylic bromination (Ford and Waters, *J.*, 1952, 2240) has been elucidated by independently showing that the radicals, RR′CX·, derived from this class of compound were able to abstract the halogen from *N*-bromosuccinimide and other "positive" halogen compounds in a manner which is analogous to that postulated in equation (2) for phenyl radicals (Ford and Waters, *loc. cit.*; Ford, Hunt, and Waters, *J.*, 1953, 3529).

The present experiments were undertaken to demonstrate the occurrence of processes (1) and (2) by isolating the products formed in the reaction between equimolar quantities of *N*-bromosuccinimide and benzoyl peroxide; the use of a solvent was dispensed with, for no

common solvent would remain unattacked. The controlled decomposition of an intimate mixture of the reactants at temperatures not exceeding 100° afforded bromobenzene (54%), succinimide (20%), benzoic acid (16%), and carbon dioxide, together with intractable material.

The isolation of bromobenzene shows that phenyl radicals do indeed abstract bromine from *N*-bromosuccinimide, and thus definitely establishes the nature of the initiation process in benzoyl peroxide catalysed allylic bromination. The conversion of succinimidyl and benzoyloxy-radicals into succinimide and benzoic acid is of some interest; no obvious hydrogen donor is present in the system, though it can be suggested that the $\cdot CH_2 \cdot CO \cdot$ grouping, which is known to be susceptible to dehydrogenation by free radicals, might be responsible for the transformation of the radicals in question into stable products.

Experimental.—*N*-Bromosuccinimide and benzoyl peroxide were recrystallised samples, having purities (iodometric) of 98% and 99%, respectively.

A finely powdered mixture of the bromo-imide (1·78 g., 0·01 mole) and the peroxide (2·42 g., 0·01 mole) was contained in a 10-ml. long-necked distillation flask which was very slowly heated with a naked flame. After 1 hr. a slurry was formed from which carbon dioxide began to be evolved; the heating was then continued in such a way that after 30 min. a golden-yellow melt resulted. By keeping the mixture just molten, at 90—100°, a slow and steady evolution of gas was maintained, the reaction being complete (negative potassium iodide–starch test) after a further 1·5 hr. The mixture was very thoroughly stirred by hand throughout the whole operation, for local overheating, particularly at the outset, led to violent explosions.

Direct distillation of the product afforded bromobenzene (0·85 g., 54%), b. p. 70°/65 mm., characterised by conversion into *p*-bromonitrobenzene, m. p. and mixed m. p. 126°. The residue was dissolved in chloroform and repeatedly shaken with aqueous sodium hydrogen carbonate. Acidification of the combined aqueous extracts followed by isolation with ether gave a brown gum; sublimation at atmospheric pressure and crystallisation of the sublimate from light petroleum (b. p. 50—60°) afforded benzoic acid (0·2 g., 16%), m. p. and mixed m. p. 121°.

In another experiment the initial product, after trituration with light petroleum, was repeatedly extracted with 20-ml. portions of boiling carbon tetrachloride; the solid which separated on each occasion was washed with ether, and the combined material was recrystallised from benzene giving succinimide (0·2 g., 20%), m. p. and mixed m. p. 124°.

THE UNIVERSITY, OLD ABERDEEN. [*Received, March 15th*, 1955.]

6-*Methoxy*-2-*naphthaldehyde*.

By R. P. GANDHI, V. S. GAIND, and S. M. MUKHERJI.

[Reprint Order No. 6239.]

6-METHOXY-2-NAPHTHALDEHYDE has been prepared in 53% yield from 2-bromo-6-methoxynaphthalene. The method is an improvement on that of Horeau and Ormancy (*Compt. rend.*, 1953, **236**, 826).

Experimental.—The Grignard reagent from 2-bromo-6-methoxynaphthalene (28·4 g.; 0·12 mole) was activated by means of ethyl bromide and then cooled in ice, and ethyl orthoformate (29·6 g.; 0·2 mole) was added during 15 min. The ether was removed and the mixture refluxed for 5 hr., cooled, and decomposed with hydrochloric acid (15%; 150 c.c.). The organic layer was washed with water, and the solvent removed under reduced pressure. The residue was gently refluxed with hydrochloric acid (20%; 100 c.c.) for 10 hr., the organic layer separated, and the aqueous layer extracted with benzene. The combined organic layers were washed twice with water and dried (K_2CO_3), and the solvent removed. 6-Methoxy-2-naphthaldehyde distilled at 140—145°/5 mm. and was purified through the bisulphite compound. The aldehyde [12 g.; 53%; from light petroleum (b. p. 60—80°)] had m. p. 81—82° (Found: C, 77·2; H, 5·2. Calc. for $C_{12}H_{10}O_2$: C, 77·4; H, 5·4%). The *oxime* had m. p. 154—155° (Found: N, 7·2. $C_{12}H_{11}O_2N$ requires N, 7·0%), the *semicarbazone*, m. p. 215° (decomp.) (Found: N, 17·2. $C_{13}H_{13}O_2N_3$ requires N, 17·3%), and the 2 : 4-dinitrophenylhydrazone, m. p. 270—271° (Found: N, 15·0. $C_{18}H_{14}O_5N_4$ requires N, 15·3%).

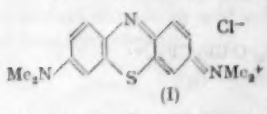
PANJAB UNIVERSITY, HOSHIARPUR, INDIA. [*Received, March 15th*, 1955.]

The Crystal Structure of Methylene-blue.

By J. O. Warwicker.

[Reprint Order No. 6240.]

In connection with an *X*-ray investigation of the combination of basic dyes with acidic oxycelluloses some measurements have been made on crystals of methylene-blue (I). *X*-Ray examination showed that the unit cell is monoclinic, with the dimensions: $a = 9{\cdot}63 \pm 0{\cdot}02$, $b = 31{\cdot}1 \pm 0{\cdot}1$, $c = 6{\cdot}96 \pm 0{\cdot}02$ Å; $\beta = 97°$. The space group is $P2_1/c$. These results are in general agreement with those reported by W. H. Taylor (*Z. Krist.*, 1935, **91**, 450; *Chem. and Ind.*, 1935, 732), but the cell dimensions differ slightly from his values.



(I)

On the assumption that the unit cell contains four dye molecules, the cell constants and the measured density of the crystals (1·31 g. cm.$^{-3}$) lead to a molecular weight of 408, which is close to the value (410) for a pentahydrate. The water content corresponding to this composition agrees closely with that obtained by drying a portion of the dye used in the *X*-ray work, and with the results of moisture determinations and chemical analyses previously made in these laboratories on a number of other recrystallized samples (Davidson, *J. Text. Inst.*, 1947, **38**, T408). On the other hand, Taylor concluded from his crystallographic data and observed density (1·29 g. cm.$^{-3}$) that his crystals contained 4 mols. of water and in the literature the dye has been formulated with from 1 to 5 mols. These discrepancies might be explained if methylene-blue chloride were capable of forming a number of hydrates stable within different humidity ranges.

It was found that within the range 0—50% r.h. the moisture content of the dye increased continuously with increasing humidity, the relation being similar to the typical adsorption isotherm. At 50% r.h. the moisture content is about 2·5 mols. of water; between 50 and 60% r.h. it rises abruptly to 5 mols., and it remains constant at this value over the range 60—96% r.h. Thus it appears that at above 60% r.h. the stable form of the dye is a pentahydrate. In drier atmospheres the equilibrium moisture content is less than that of the pentahydrate, but no evidence of the existence of a tetrahydrate, or other lower hydrate, has been obtained.

Taylor (*loc. cit.*) also found the bromide of methylene-blue and of its selenium analogue to be isomorphous with methylene-blue chloride. In view of this, it is interesting that he concluded that the bromides crystallized with 5 molecules of water.

Experimental.—Methylene-blue chloride was salted out with sodium chloride from a concentrated aqueous solution of a commercial product, and then recrystallized twice from water; it was dried by exposure to the air at the ordinary temperature. Crystals for *X*-ray work were obtained by slow evaporation of a cold saturated aqueous solution of the purified dye. As was noted by Taylor, the crystals show twinning, but it was possible to cut untwinned fragments from the larger crystals.

The density of the crystals was determined by flotation with benzene–carbon tetrachloride. The value obtained (1·31 g. cm.$^{-3}$) was confirmed by pycnometric measurements in benzene at 20°.

The unit-cell dimensions were obtained from oscillation photographs by an extrapolation method based on that of Farquhar and Lipson (*Proc. Phys. Soc.*, 1946, **58**, 200); the angle β was obtained from a Weissenberg photograph.

The relation between the moisture content of the dye and the relative humidity was determined by first drying samples over phosphoric oxide and then exposing them to atmospheres of known relative humidity at 20° until the weight was constant. The relative humidity was controlled by means of solutions of sulphuric acid (Wilson, *J. Ind. Eng. Chem.*, 1921, **13**, 326). At 60% r.h. the moisture content was 21·4% and in the range 70—96% r.h. it varied between 21·9 and 22·2% (Calc. for $C_{16}H_{18}N_3SCl,5H_2O$: H_2O, 22·0%).

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[*Received, March 16th*, 1955.]

Perfluoroalkyl Derivatives of Nitrogen. Part II. Bisperfluoroalkylamines.*

By D. A. Barr and R. N. Haszeldine.

[Reprint Order No. 6248.]

A general method for the conversion of perfluoroalkylnitroso-compounds into perfluoro(alkylalkyleneamines) was described in Part I *, *e.g.*:

$$CF_3{\cdot}NO + C_2F_4 \longrightarrow CF_3{\cdot}\overbrace{N{\cdot}O{\cdot}CF_2{\cdot}CF_3} + -[N(CF_3){\cdot}O{\cdot}CF_2{\cdot}CF_2]_n-$$

$$\downarrow \text{Pyrolysis}$$

$$\text{(I)}\quad CF_3{\cdot}N{:}CF_2 + COF_2$$

The availability of perfluoro(alkylalkyleneamines) now opens up a convenient general route to bisperfluoroalkylamines, and particularly to (perfluoroalkyl)trifluoromethylamines, since the C:N in the system $-CF_2{\cdot}N{:}CF-$ reacts readily with anhydrous hydrogen fluoride:

$$CF_3{\cdot}[CF_2]_m{\cdot}N{:}CF{\cdot}[CF_2]_n{\cdot}CF_3 \xrightarrow{HF} CF_3{\cdot}[CF_2]_n{\cdot}NH{\cdot}CF_2{\cdot}[CF_2]_m{\cdot}CF_3$$

$$CF_3{\cdot}[CF_2]_n{\cdot}N{:}CF_2 \xrightarrow{HF} CF_3{\cdot}[CF_2]_n{\cdot}NH{\cdot}CF_3$$

$$\textit{e.g.},\quad \underset{\text{(I)}}{CF_3{\cdot}N{:}CF_2} + HF \longrightarrow (CF_3)_2NH$$

The chemistry of unsubstituted alkylalkyleneamines has been investigated only in outline. They are said to combine readily with bromine or iodine to give solids believed to be dihalides: $R{\cdot}CH{:}NR' \xrightarrow{X_2} R{\cdot}CHX{\cdot}NXR'$ (X = Br or I; R = alkyl; R' = alkyl or H), but no proof of structure is available (Franchimont and Van Epps, *Rec. Trav. chim.*, 1896, **15**, 169; Berg, *Bull. Soc. chim. France*, 1925, **37**, 637; Turcan, *ibid.*, 1932, **51**, 486; Dains and Lehmann, *Trans. Kansas Acad. Sci.*, 1931, **34**, 297; *Chem. Abs.*, 1932, **26**, 5270; Shelton, U.S.P. 2,393,271; *Chem. Abs.*, 1946, **40**, 2273). Delépine (*Bull. Soc. chim. France*, 1903, **29**, 1200) showed that hydrogen cyanide reacted by addition with the compound EtN:CHMe to give Et·NH·CHMe·CN, but the reaction of hydrogen halides with alkyleneamines has apparently not been investigated. Pearlson and Hals (U.S.P. 2,643,267; *Chem. Abs.*, 1954, **48**, 6461) have recently briefly stated that hydrogen fluoride reacts with "fluorocarbon azomethines," *i.e.*, perfluoro(alkylalkyleneamines), to give *sec.*-perfluoroamines, but details of conditions, yields, or products have not yet been released.

Perfluoro(methylmethyleneamine) (I) fails to react with chlorine at room temperature, and is recovered unchanged when heated with iodine. This sharp contrast with unsubstituted alkylalkyleneamines is not unexpected in view of the marked differences between addition reactions of olefins and the corresponding perfluoro-olefins (*e.g.*, $CH_3{\cdot}CH{:}CH_2$ and $CF_3{\cdot}CF{:}CF_2$). Reaction of perfluoro(methylmethyleneamine) with anhydrous hydrogen fluoride proceeds smoothly and almost quantitatively at 150°, however, and yields bistrifluoromethylamine (b. p. −6·7°). This is the first bisperfluoroalkylamine to be prepared by an unambiguous route, although the same compound was believed to be formed during the reaction of iodine pentafluoride with iodine cyanide (Ruff and Willenberg, *Ber.*, 1940, **73**, 724). The hydrogen for this last reaction was presumably supplied as hydrogen fluoride by moisture entering the reaction as impurity and combining with the iodine pentafluoride. The boiling point of the by-product obtained by Ruff and Willenberg (−6·2°) is in fact close to that of pure bistrifluoromethylamine; but, if the two compounds are identical, the mechanism of formation of bistrifluoromethylamine from iodine cyanide is, at first sight, obscure.

Bistrifluoromethylamine is a colourless gas, whose infrared spectrum shows a strong N–H stretching absorption at 2·89 μ (see Barr and Haszeldine, *J.*, 1955, in the press, for a discussion of the infrared spectrum). The gas is quite stable in absence of moisture, but

* Part I, *J.*, 1955, 1881, where references to earlier related work are given.

is rapidly converted by water into carbon dioxide and fluoride and ammonium ions; this is essentially hydrolysis under acid conditions. Decomposition in alkaline solution also causes complete breakdown of bistrifluoromethylamine, but the nitrogen appears as cyanate ion and not as ammonium ion. Perfluoro(methylmethyleneamine) gives analogous products, *i.e.*, ammonium ion in acid solution, cyanate ion in alkaline solution, and it is thus probable that bistrifluoromethylamine decomposes by initial loss of hydrogen fluoride to give perfluoro(methylmethyleneamine). Cyanate ion is converted into ammonium ion and carbon dioxide in acid solution, so a common mechanism can be written for both acid and base hydrolyses:

$$(CF_3)_2NH \longrightarrow HF + CF_2{\cdot}N{:}CF_2 \xrightarrow{H_2O} CF_3{\cdot}NH_2 + COF_2$$

$$CF_3{\cdot}NH_2 \xrightarrow{-HF} CF_2{:}NH \xrightarrow{-HF} FCN \xrightarrow{OH^-} HOCN$$

$$CF_2{:}NH \xrightarrow{OH^-} HNCO \qquad FCN \rightleftarrows HNCO$$

$$HNCO + H_2O + H^+ \longrightarrow CO_2 + NH_4^+$$

If Ruff and Willenberg's by-product (which also yielded cyanate ion in alkaline solution) is in fact bistrifluoromethylamine, then a possible route to it is by reversal of the hydrolysis reaction, *i.e.*, by reaction of trifluoromethylamine with carbonyl fluoride produced by oxidative breakdown of iodine cyanide:

$$IF_5 \xrightarrow{H_2O} HF + IOF_3$$

$$ICN \xrightarrow{IOF_3} COF_2$$

$$ICN \xrightarrow{IF_5} FCN \underset{2HF}{\rightleftharpoons} CF_3{\cdot}NH_2 \xrightarrow{COF_2} CF_3{\cdot}N{:}CF_2 \xrightarrow{HF} (CF_3)_2NH$$

Confirmation of this must await the synthesis of trifluoromethylamine.

Experimental.—Perfluoro(methylmethyleneamine) was prepared by reaction of trifluoronitrosomethane with tetrafluoroethylene, followed by pyrolysis of the products (Part I, *loc. cit.*); its purity was checked by infrared spectroscopic examination.

Attempted addition reactions with perfluoro(methylmethyleneamine). (*a*) Perfluoro(methylmethyleneamine) (0·050 g., 0·00038 mole) and anhydrous chlorine (0·024 g., 0·00034 mole) were immiscible at room temperature, and failed to react during 3 days in a sealed 5-ml. Pyrex tube.

(*b*) The unsaturated compound (0·066 g.) and iodine (0·120 g.), heated at 160° (20 hr.) in a sealed tube, underwent no reaction.

Bistrifluoromethylamine. Perfluoro(methylmethyleneamine) (12·15 g., 0·0914 mole) and anhydrous hydrogen fluoride (1·75 g., 0·0875 mole) in a 20-ml. steel autoclave (pretreated with anhydrous hydrogen fluoride) were heated at 150° (15 hr.). Fractionation of the volatile products *in vacuo* gave *bistrifluoromethylamine* (12·4 g., 0·0810 mole, 89%) (Found: C, 15·8; H, 0·6; N, 9·2%; *M*, 154. C_2HNF_6 requires C, 15·7; H, 0·65; N, 9·2%; *M*, 153), unchanged perfluoro(methylmethyleneamine) (0·007 g., 0·05%), and negligible amounts of carbon dioxide, hydrogen fluoride, and silicon tetrafluoride. The formation of bistrifluoromethylamine is probably quantitative, since slight losses occurred during manipulation.

The vapour pressure of bistrifluoromethylamine, measured over the temperature range −66° to −8°, is given by the equation $\log_{10} p = 7{\cdot}896 - 1335/T$ (p in mm., T in °K), whence the b. p. is calculated as −6·7°, Trouton's constant is 22·9, and the latent heat of vaporisation is 6100 cal./mole.

Hydrolysis of bistrifluoromethylamine. (*a*) The amine (0·050 g., 0·000325 mole) and water (0·5 ml.) reacted immediately in a sealed 5-ml. Pyrex tube. After 12 hr., fractionation of the volatile products gave carbon dioxide (0·028 g., 0·000652 mole, 100%) (Found: *M*, 44. Calc. for CO_2: *M*, 44). The aqueous solution contained fluoride and ammonium ions.

(*b*) The amine (0·103 g., 0·00067 mole) and 10% aqueous sodium hydroxide (5 ml.), shaken in a sealed 25-ml. Pyrex tube at room temperature (4 hr.), gave only fluoride, carbonate, and cyanate ions. Ammonia was not detectable as gaseous product. Cerous nitrate–acetic acid was used to test for fluoride, and copper sulphate–pyridine for the cyanate test.

Alkaline hydrolysis of perfluoro(methylmethyleneamine). A rapid reaction ensued when

perfluoro(methylmethyleneamine) (0·062 g., 0·00047 mole) and 10% aqueous sodium hydroxide (5 ml.) were sealed in a 25-ml. Pyrex tube and shaken at room temperature (5 hr.). No volatile products were found, and in particular ammonia was absent. Tests on the aqueous solution revealed the presence of fluoride, carbonate, and cyanate ions.

One of us (D. A. B.) is indebted to Imperial Chemical Industries Limited, Plastics Division, for a Maintenance grant.

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Attempted Synthesis of 9 : 10-*Dihydro*-7 : 8 : 2′ : 3′-*tetramethoxy*-10-*methyl*-1 : 2-*benzophenanthridine by the Pschorr Reaction.*

By T. R. GOVINDACHARI and N. ARUMUGAM.

[Reprint Order No. 6254.]

As the first step in the synthesis named in the title, 1 : 2 : 3 : 4-tetrahydro-1-hydroxyimino-6 : 7-dimethoxynaphthalene (Haworth and Mavin, *J.*, 1932, 1485) was reduced to the 1-amine by sodium amalgam. When heated with formic acid this amine did not give the expected formyl derivative but, instead, the amino-group was eliminated with formation of a neutral nitrogen-free oil. The acetyl derivative of the amine was, however, easily obtained and was dehydrogenated by heating it in *p*-cymene with palladised charcoal to *N*-acetyl-6 : 7-dimethoxy-1-naphthylamine; a side reaction led to the simultaneous formation of 2 : 3-dimethoxynaphthalene. The amine obtained from the acetyl derivative by hydrolysis was formylated and then reduced by lithium aluminium hydride to 6 : 7-dimethoxy-*N*-methyl-1-naphthylamine, which condensed with 2 : 3-dimethoxy-6-nitrobenzoyl chloride to yield *N*-(2 : 3-dimethoxy-6-nitrobenzoyl)-6 : 7-dimethoxy-*N*-methyl-1-naphthylamine, though only in 30% yield. The amide was reduced catalytically to *N*-(6-amino-2 : 3-dimethoxybenzoyl)-6 : 7-dimethoxy-*N*-methyl-1-naphthylamine which was then submitted to the Pschorr reaction, under a variety of conditions. Careful chromatography of the products failed to yield any crystalline material.

Experimental.—**1 : 2 : 3 : 4-*Tetrahydro*-6 : 7-*dimethoxy*-1-*naphthylamine*.** Sodium amalgam (400 g.) was added in small portions to a solution of 1 : 2 : 3 : 4-tetrahydro-6 : 7-dimethoxy-1-hydroxyiminonaphthalene (20 g.) in alcohol (200 ml.) at 60°. The solution was kept acidic by intermittent addition of 50% acetic acid. After 3 hr. the mercury was removed and the alcohol distilled off *in vacuo*. The residue was made alkaline and extracted with ether. On removal of the ether from the dried extract, the base was obtained as an oil (18 g.). This was heated with acetic anhydride (15 ml.) and the *acetyl derivative* produced was recrystallised from benzene–light petroleum, yielding needles, m. p. 149° (Found: C, 67·7; H, 7·5; N, 5·3. $C_{14}H_{19}O_3N$ requires C, 67·5; H, 7·6; N, 5·6%).

N-*Acetyl*-6 : 7-*dimethoxy*-1-*naphthylamine*. The foregoing acetyl derivative (2 g.) was heated in *p*-cymene under reflux with 30% palladised charcoal (0·2 g.) for 8 hr. in a carbon dioxide atmosphere. The hot solution was filtered. The filtrate deposited, on cooling, white needles (1·2 g.) which on recrystallisation from benzene yielded N-*acetyl*-6 : 7-*dimethoxy*-1-*naphthylamine* (0·9 g.), m. p. 185° (Found: C, 68·3; H, 6·2; N, 5·8. $C_{14}H_{15}O_3N$ requires C, 68·6; H, 6·1; N, 5·7%). From the benzene mother-liquor undehydrogenated substance (0·3 g.) was recovered. The *p*-cymene filtrate yielded on concentration 2 : 3-dimethoxynaphthalene, m. p. 116° (Kauffmann and Beisswenger, *Ber.*, 1903, **36**, 569).

6 : 7-*Dimethoxy*-1-*naphthylamine*. The acetyl derivative (5 g.) in refluxing 20% sulphuric acid (200 ml.; 3 hr.) gave the *base*, m. p. 130° (from alcohol) (Found: C, 71·3; H, 6·1; N, 7·2. $C_{12}H_{13}O_2N$ requires C, 70·9; H, 6·4; N, 6·9%). This (5 g.) was heated with formic acid (6 ml.; 90%) for 3 hr. at 180°. The *formyl derivative*, crystallised from alcohol, melted at 175° (Found: C, 67·7; H, 5·4; N, 6·2. $C_{13}H_{13}O_3N$ requires C, 67·5; H, 5·6; N, 6·1%).

6 : 7-*Dimethoxy*-N-*methyl*-1-*naphthylamine*. The formyl derivative (2 g.) was added to lithium aluminium hydride (2 g.) in tetrahydrofuran (100 ml.). After 2 hours' stirring the excess of hydride was decomposed by water, and the solution decanted from the alumina, which was further washed with ether. The solvent was removed *in vacuo* and the residual *base* crystallised from methanol, yielding needles (1 g.), m. p. 154° (Found: C, 72·1; H, 6·4; N, 6·3. $C_{13}H_{15}O_2N$ requires C, 71·9; H, 6·9; N, 6·5%).

This amine (1·3 g.) in benzene (30 ml.) was treated with 10% potassium carbonate solution

(30 ml.) and then with a solution of 2 : 3-dimethoxy-6-nitrobenzoyl chloride (1·8 g.) in benzene (30 ml.) with vigorous stirring. After an hour the benzene layer was separated, washed successively with dilute hydrochloric acid, dilute sodium hydroxide solution, and water, dried, concentrated to a small volume, and poured on to an alumina column, which was then eluted with benzene. From the eluate, the 2 : 3-*dimethoxy-6-nitrobenzoyl derivative* was obtained in 30% yield, m. p. 216° (Found : C, 62·1 ; H, 5·1 ; N, 6·3. $C_{22}H_{22}O_7N_2$ requires C, 62·0 ; H, 5·2 ; N, 6·6%).

N-(*6-Amino*-2 : 3-*dimethoxybenzoyl*)-6 : 7-*dimethoxy*-N-*methyl*-1-*naphthylamine*. The nitro-compound (1 g.) in alcohol (25 ml.) was reduced in the presence of Adams catalyst. The *product* (0·6 g.), crystallised from methanol, had m. p. 154° (Found : C, 67·2 ; H, 6·1 ; N, 7·0. $C_{22}H_{24}O_5N_2$ requires C, 66·7 ; H, 6·0 ; N, 7·1%). The *hydrochloride* crystallised from absolute alcohol and melted with decomposition at 215° (Found : C, 60·7 ; H, 6·3. $C_{22}H_{25}O_5N_2Cl$ requires C, 61·0 ; H, 6·5%).

We are grateful to the Government of India and to the East India Pharmaceuticals Works Ltd., Calcutta, for the award of a scholarship to one of us (N. A.), and to Mr. S. Selvavinayagam for the microanalyses.

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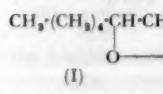
Madras 5, India. [*Received, March 21st*, 1955.]

Synthesis of (±)-*Massoialactone.*

By L. Crombie.

[Reprint Order No. 6279.]

Massoi bark (from *Cryptocarya massoia*, family Lauraceae) on steam distillation yields about 2% of an essential oil from which an optically active unsaturated lactone, massoia (or massoy)lactone, has been isolated (Abe, *J. Chem. Soc. Japan*, 1937, **58**, 246 ; Meijer, *Rec. Trav. chim.*, 1940, **59**, 191). Abe formulated it as (−)-7-methyl-non-2-eno-5-lactone but Meijer, on the basis of oxidative degradation, has shown it to be (−)-dec-2-eno-5-lactone (I). Abe and Sato (*J. Chem. Soc. Japan*, 1954, **75**, 952) now concur with Meijer.



(I)

A synthesis of (±)-dec-2-eno-5-lactone was recently described in connection with the preparation of deca-*cis*-2 : *trans*-4-dienoic acid (Crombie, *J.*, 1955, 1007). Through the intercession of Dr. Meijer, Dr. Boeknoogen has generously provided an authentic specimen of massoialactone ; its infrared spectrum (liquid film) is identical with that of the synthetic material. Meijer's structure for the natural lactone is thus firmly established. As expected, the (−)-lactone in 0·01N-methanolic sodium methoxide has initially only pronounced end absorption, but gradually develops a maximum at 260 mμ. This is due to intramolecular elimination giving sodium deca-*cis*-2 : *trans*-4-dienoate. Data for massoialactone and synthetic (±)-dec-2-eno-5-lactone are summarised in the table.

						Infrared	
Natural (−)	B. p.	n_D^t	d_4^t	R_D^1	$[\alpha]_D^t$	C=O	C=C
Abe	122—123°/2 mm.	1·4718 (20°)	0·9859 (20°)	47·76	−97° [3]	—	—
Meijer	169·5—174/24 mm.	1·4714 (26)	0·9788 (27·5)	48·02 [2]	−93 [3]	—	—
Crombie [4] ...	103—104/0·5 mm.	1·4722 (21)	0·9800 (21)	48·09	−95·5 [4]	1723 s [5]	1627 w
Synthetic (±)							
Crombie [7].....	85—86/0·07 mm.	1·4705 (21)	0·9785 (21)	48·01	0	1723 s [5]	1627 w

[1] Calc. molecular refractivity, 47·37 (data from Gilman, "Organic Chemistry," Wiley, 1943, Vol. II, p. 1751). [2] n_D corrected to 27·5° by −0·0004 per degree for this calculation. [3] Neat liquid. [4] *c*, 10·42% in ethanol. [5] Pinder, *J.*, 1952, 2236, gives 1725 cm.$^{-1}$ for hex-2-eno-5-lactone. [6] Dr. Boeknoogen's specimen had n_D^{18} 1·4727 and was redistilled. [7] *Loc. cit.*

Both the natural and the synthetic lactone have similar characteristic odours and irritate the skin. Massoi bark is used in native medicine in Dutch New Guinea and in view of the interesting physiological activity of hex-2-eno-5-lactone (see Haynes, *Quart. Rev.*, 1948, **2**, 48 ; *idem*, "Modern Methods of Plant Analysis," Vol. II, Springer, Berlin, 1955, p. 583) specimens are being tested by Dr. L. J. Haynes.

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South Kensington, London, S.W.7. [*Received, March 30th*, 1955.]

The Preparation of Some Derivatives of 5 : 6-Dimethoxyindole.

By D. G. Harvey.

[Reprint Order No. 6299.]

During metabolic studies some derivatives of 5 : 6-dimethoxyindole were required. Oxford and Raper (*J.*, 1927, 417) prepared this by the ferrous sulphate reduction of 4 : 5-dimethoxy-2-nitrophenylpyruvic acid in poor yield. If, however, the concentration of ammonia was increased and the ferric oxide sludge thoroughly washed with aqueous ammonia, reasonable yields resulted. In addition, the pyruvic acid need not be isolated, but can be used as an ammoniacal solution of the potassium salt. Decarboxylation of 5 : 6-dimethoxyindole-2-carboxylic acid was effected smoothly in glycerol. Attempts to introduce an aldehyde group into 5 : 6-dimethoxyindole, including the Reimer–Tiemann, Gattermann, and gramine reactions, failed. However, the Gattermann reaction with ethyl indole-2-carboxylate gave (cf. Boyd and Robson, *Biochem. J.*, 1935, **29**, 555) the aldimine and thence the aldehyde. Attempts to decarboxylate this compound resulted in tars.

Experimental.—*5 : 6-Dimethoxyindole-2-carboxylic acid.* A suspension of the potassium derivative of ethyl 5 : 6-dimethoxy-2-nitrophenylpyruvate was prepared from 4 : 5-dimethoxy-2-nitrotoluene as described by Oxford and Raper (*loc. cit.*). This was shaken out with water (500 ml.) and the benzene–ether layer extracted with 7% aqueous ammonia (75 ml. × 10). A further quantity of ammonia (125 ml.; *d* 0·880) was added to the combined aqueous extracts. Hot ferrous sulphate solution (500 g. in 800 ml. of water) was added and the mixture heated on water-bath for 0·5 hr. and boiled for the same length of time. The ferric oxide sludge was boiled five times with 3·5% aqueous ammonia (1 l. per time). The combined filtrates were decolorised with charcoal at 80° and concentrated *in vacuo*. Acidification of the cold concentrate (Congo-red) with 5% sulphuric acid yielded practically colourless needles of the indole acid. Recrystallisation from ethanol or acetic acid gave colourless needles, m. p. 223° (decomp.) (20—23 g., 35—41% based on nitrotoluene) (Found : N, 6·3. Calc. for $C_{11}H_{11}O_4N$: N, 6·3%).

5 : 6-Dimethoxyindole. The 2-carboxylic acid (20 g.) was converted into the ammonium salt by dissolution in ammonia and ethanol and concentration. The dry salt was heated in glycerol (10 ml.) at 200—210° for 0·5 hr. The hot melt was poured into excess of aqueous sodium hydrogen carbonate and cooled at 0° for 6 hr. The crystalline product (15 g., 97%), recrystallised from benzene, had m. p. 142° (Oxford and Raper give 154°). Further crystallisations and vacuum-distillation failed to raise the m. p. (Found : N, 7·8. Calc. for $C_{10}H_{11}O_2N$: N, 8·1%).

Ethyl 5 : 6-dimethoxyindole-2-carboxylate. The acid (15 g.) was converted into the ammonium salt and thence into the silver salt which was dried in *vacuo* (H_2SO_4) (21 g., 95%), then boiled in dry benzene (100 ml.) with ethyl iodide (13·5 g.) for 0·5 hr. The iodide was filtered off and washed with hot benzene, and the filtrate and washings were concentrated to 20 ml. Light petroleum (b. p. 40—80°) (100 ml.) was added. Pale yellow needles of the ester crystallised at 0° (9—10 g., 53—59%). On recrystallisation from ethyl acetate it softened at 155° and had m. p. 160° (Found : N, 5·5. Calc. for $C_{13}H_{15}O_4N$: N, 5·7%). Perkin and Rubinstein (*J.*, 1926, 357) give 172°.

Treating the carboxylic acid with excess of ethanol containing 3% v/v of sulphuric acid gave the ester (10—20%) as pale yellow-brown needles, m. p. 162°.

Anil of 3-formyl-5 : 6-dimethoxyindole-2-carboxylic acid. Ethyl 5 : 6-dimethoxyindole-2-carboxylate (5·5 g.), zinc cyanide (5·5 g.), dry ether (100 ml.), and dry chloroform (100 ml.) were treated, with stirring at 0°, with dry hydrogen chloride for 3 hr., then for 2 hr. at room temperature. The supernatant fluid was decanted, and the yellow aldimine washed with dry ether and boiled with water. The yellow crystals were warmed in ethanol with dilute aqueous sodium hydroxide (1·5 mol.) on the water-bath for 0·25 hr. and treated with aniline (1·5 mols., redistilled). After clarification with charcoal, the alcohol was removed *in vacuo*, and the solution acidified with dilute sulphuric acid (litmus). The yellow needles of the *anil*, recrystallised from ethanol and from dioxan (3·75 g., 29·0%), had m. p. 257° (Found : C, 65·3; H, 4·9; N, 18·8. $C_{18}H_{16}N_2O_4$ requires C, 66·6; H, 4·9; N, 8·6%). Treating this with dilute sulphuric acid and then with phenylhydrazine hydrochloride and sodium acetate gave the *phenylhydrazone* as yellow needles (from ethanol), m. p. 220° (Found : C, 63·7; H, 5·0. $C_{18}H_{17}O_4N_3$ requires C, 63·8; H, 4·8%).

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2-Amino-5-nitrobenzotrifluoride	9/- D
Antipyrine (phenazone)	75/- K
1 : 2-Bis β-chlorethoxyethane ($(CH_2{\cdot}O{\cdot}CH_2CH_2Cl)_2$)	9/- D
1-Butyn-3-ol (Methylethynyl carbinol)	25/- H
Chondroitin sulphate (potassium salt) (N = 2·95 %)	13/- G
Crotyl alcohol (1-hydroxy-2-butylene)	30/- D
Cyanamide	28/- K
Cytidine sulphate (chromatographically purified)	136/- G
1 : 2-Dichloro-2-fluoropropane	7/- D
7 : 8-Dihydro-linalool (96 %)	85/- H
Dihydrothymine	13/- G
1 : 4-Dihydroxy-naphthalene	65/- H
Diphenyl phosphorochloridate	18/- H
1-Ethyl-4-nitrobenzene	32/- H
Ethyl papaverine	90/- H
N-Ethyl-*N*-phenyl benzylamine	16/- H
p-Fluoro-aniline	118/- H
3-Hexyn-2 : 5-diol	13/- H
Kojic acid	90/- D
Mellitic acid (benzene hexacarboxylic acid)	12/- G
2-Naphthylamine-7-sulphonic acid	10/- H
Neopentyl glycol (2 : 2-dimethylpropanediol-1 : 3)	12/- H
3-Nitro-*p*-aminoacetanilide (96 %)	6/- H
3-Nitro-4-aminobenzotrifluoride	10/- D
3-Nitro-4-chlorobenzotrifluoride	9/- D
2-Nitro-5-chlorobenzotrifluoride	9/- D
D-Norvaline	12/- G
L-Norvaline	11/- G
D-sec-Octyl alcohol	58/- D
L-sec-Octyl alcohol	52/- D
3-Pentyn-2 : 5-diol	20/- H
Phenylethynyl carbinol-1	35/- H
Protoveratrin A or B	98/- G
DL-iso-Serine	12/- G
DL-Thyronin	48/- G
Tyrosinase (1,000 Miller-Dawson units/mg.) (5 mg. amps.)	122/- amp.

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Here, in the first number of 'Chemical News' published nearly a hundred years ago, the eventual development of scientific control of the methods and means of production is welcomed perhaps a little prematurely; but in thousands of industrial laboratories today 'the unerring laws of chemistry', and B.D.H. reagents, enable the conduct of the chemical arts to be successful and economical . . . and as civil as you please.

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